AEROSOL DEPOSITION IN THE HUMAN RESPIRATORY TRACT

by

RICHARD G. LOVE

Thesis for the Degree of Doctor of Philosophy
University of Edinburgh
1973

A B S T R A C T

This thesis describes the individual variations in the fractional deposition of 1μ diameter aerosols in the lungs of a group of 58 coal-workers. An approximately uniform aerosol was produced in a modified La Mer-Sinclair generator and the concentration was monitored by an optical means. Each subject breathed at a fixed frequency of 15 breaths per minute but the tidal volumes varied according to the energy expenditure of the subject, who pedalled a variable workload ergometer. Deposition was calculated for each workload. It was found that there was no difference in total deposition between miners with simple pneumoconiosis and a matched group without pneumoconiosis. There was a wide range of deposition values within each group, however, when these were standardised for tidal volume and breathing frequency.

Deposition was shown to be significantly correlated with FEV_1 but more significantly correlated with measurements of maximum expiratory flow in the mid-vital capacity range during an FVC manoeuvre ($MEF_{50\%}$ and $MMEF_{50-75\%}$). However the slope of deposition upon FEV_1 was not steep and, although there was a tendency for deposition to be higher in smokers than non-smokers no significant relationship could be found between deposition and occurrence of respiratory symptoms, age or years worked underground.

It was found possible to qualify the deposition pattern for each subject by a visual grading of the shape of the expired aerosol concentration curve, which was shown to change progressively from a convex to a concave shape as lung function deteriorated. The shape of this curve is believed to reflect the manner in which inspired particles are handled by the lung and also the site at which these particles are deposited.

It is suggested that increased deposition of 1μ diameter particles may occur because of obstruction or narrowing of the airways. The distribution of particles in the expired air was abnormal in smokers, and subjects who reported excess respiratory symptoms. Subjects with abnormal expired aerosol concentration curves had significantly higher deposition and lower $MMEF_{50-75\%}$ compared with subjects who had the normal aerosol curves which are characteristic of most non-smoking subjects.

The results of this study indicate that increased deposition of inhaled dust is unlikely to be a factor in the development of simple pneumoconiosis, nor does the presence of pneumoconiosis cause total deposition to be increased.

CONTENTS

ILLUSTRATIONS AND TABLES

TABLES

TABLES

CHAPTER 1

INTRODUCTION

During the mining of coal a considerable amount of airborne dust is produced, from which the underground worker must be protected. One aspect of this problem is to determine the interaction of the various factors concerned in the aetiology of coal workers' pneumoconiosis and the individual variations which influence the course of the disease.

The particular aspect to be presented in this thesis concerns the rate of deposition of inhaled dust in the respiratory tract and its relationship to pneumoconiosis. It is the purpose of this work to investigate the individual variation in the amounts of dust deposited in the lungs of human subjects with special reference to simple pneumoconiosis of coalworkers.

1.1. The fate of inhaled dust

When dust is inhaled into the respiratory system the particles, governed by physical laws, deposit in the upper or lower airways depending on the pattern of breathing and properties of the particles. The principle factor governing the site of deposition of inhaled dust is the size of the particles.. This determines the percentage of the dust which will be deposited in each region of the lung by means of the three forces affecting deposition: impaction, sedimentation and diffusion. These factors were first analysed by Findeisen (1935).

For spheres:

(1) Inertial impaction occurs when a particle is moving in an airstream which undergoes a sudden change of direction. Because of its inertia the particle tends to continue on its original path and impact on the wall of the airway. The sideways slip of the particle is resisted by air friction but the probability of impaction is proportional to the density of the particle and to the square of its diameter and is also a function of the velocity of the airflow and angle of the bend. It is an important force of deposition for particles greater than 5μ in diameter but decreases to neglible proportions for particles smaller than 1μ in diameter. Impaction probably

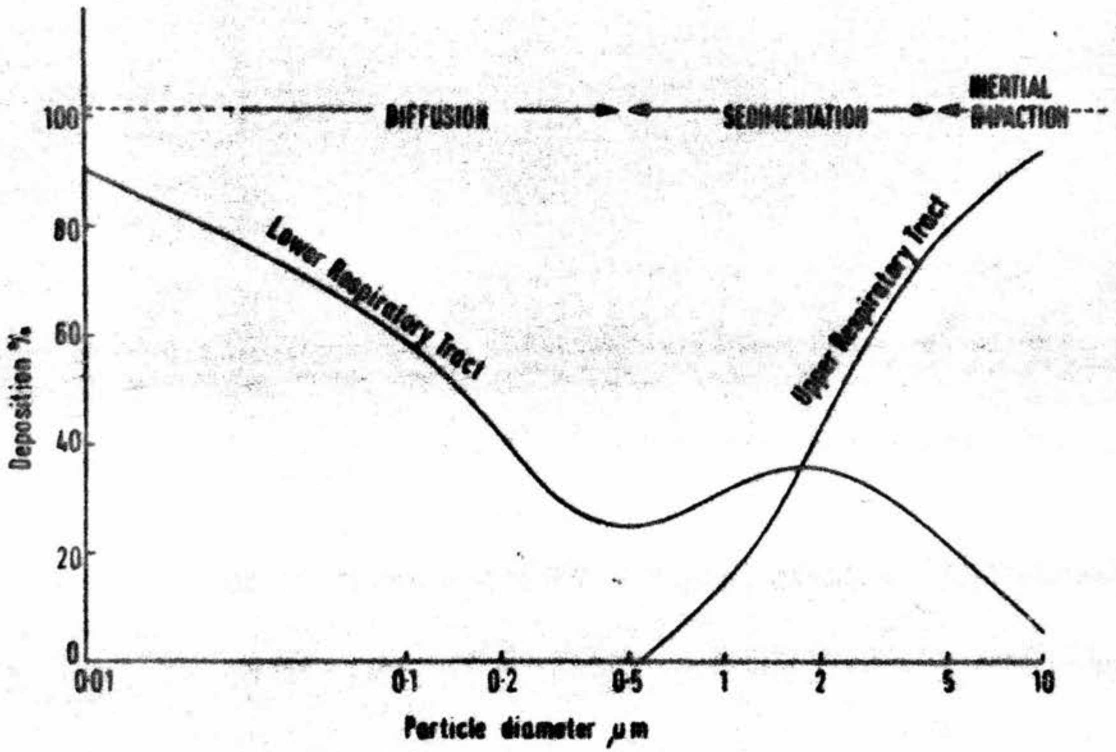

Fig. 1 Effect of particle diameter on total deposition of aerosol in the respiratory tract, showing the approximate size range over which the three principal forces of deposition are most effective. (re-drawn from Morrow, P.E. (1967)).

approaches a maximum in the 5th or 6th generation of airways (Landahl, 1950).

(2) A particle suspended in air or in a moving airstream will fall under the influence of gravity at a rate which is proportional to its density and to the square of its diameter. This process, called sedimentation, is an important factor in deposition especially for particles in the range 0.5 - 5μ, and its effects are greatest in narrower airways where the average distance which the particle must fall before it reaches the wall is smaller.

(3) Deposition due to diffusion or Brownian motion is dependent on the kinetic energy of gas molecules, which constantly bombard the airborne particles. The effects of this process are greatest for small particles and is insignificant for those $>$ 0.5μ in diameter. The probability of a particle depositing by diffusion increases in inverse proportion to its diameter. It is independent of the density of the particle.

During breathing the overall deposition of inhaled particles of any particular size will be affected predominantly by one or a combination of two of the factors outlined above. Large particles are deposited mainly by impaction and sedimentation in the upper airways and very small particles with a high coefficient of diffusion are deposited with a similar pattern. Particles of an intermediate size are able to penetrate to the lower respiratory tract and may be deposited within the alveoli. The site and extent of deposition is therefore primarily dependent on particle size and this is illustrated in graphical form in Fig.1. However, most inhaled dusts are polydisperse, i.e. consist of a wide range of particle sizes, so that it is important to consider the relative number of particles in each size range. In an ordinary dust cloud it is not uncommon to find that 90% of the particles constitute only 10% or less of the mass.

Many industrial dust clouds are made up of particles of irregular shape caused by the processes of fragmentation and the individual particles are frequently aggregated. The measured diameter of particles of quartz, coal, clay etc., may be up to twice the diameter of a unit density sphere having the same settling velocity as the particle in question (equivalent aerodynamic diameter). Therefore

TABLE 1

Dimensions of Human Airway Model (Regular dichotomous branching).
Average adult lung with volume 4800 ml at about $\frac{3}{4}$ maximal inflation.*

Generation	Number per generation n	Diameter (cm)	Length (cm)	Total Cross Section (cm^2)	Total Volume (cm^3)	Accumul. Volume (cm^3)
0	1	1.8	12.0	2.54	30.50	30.5
1	2	1.22	4.76	2.33	11.25	41.8
2	4	0.83	1.90	2.13	3.97	45.8
3	8	0.56	0.76	2.00	1.52	47.2
4	16	0.45	1.27	2.48	3.46	50.7
5	32	0.35	1.07	3.11	3.30	54.0
6	64	0.28	0.90	3.96	3.53	57.5
7	128	0.23	0.76	5.10	3.85	61.4
8	256	0.186	0.64	6.95	4.45	65.8
9	512	0.154	0.54	9.56	5.17	71.0
10	1,024	0.130	0.46	13.4	6.21	77.2
11	2,048	0.109	0.39	19.6	7.56	84.8
12	4,096	0.095	0.33	28.8	9.82	94.6
13	8,192	0.082	0.27	44.5	12.45	106.0
14	16,384	0.074	0.23	69.4	16.40	123.4
15	32,768	0.066	0.20	113.0	21.70	145.1
16	65,536	0.060	0.165	180.0	29.70	174.8
17	131,072	0.054	0.141	300.0	41.80	216.6
18	262,144	0.050	0.117	534.0	61.10	277.7
19	524,288	0.047	0.099	944.0	93.20	370.9
20	1,048,576	0.045	0.083	1,600.0	139.50	510.4
21	2,097,152	0.043	0.070	3,220.0	224.30	734.7
22	4,194,304	0.041	0.059	5,880.0	350.00	1,084.7
23	8,388,608	0.041	0.050	11,800.0	591.00	1,675.0

*Taken from Weibel, E.R. Morphometry of the Human Lung, Berlin: Springer, 1963.

the shape and density of particles in a dust cloud must be considered in an analysis of the respiratory deposition of inhaled particles.

The pattern of breathing modifies the respiratory depostion of dust. An increased breathing frequency will reduce the residence time of air-borne particles in the lung, thus allowing the forces of diffusion and sedimentation a shorter interval during which to act. The greater velocity of airflow which is caused by an increase in the minute volume, however, will increase the probability of deposition of larger particles by impaction. Conversely deeper tidal volumes allow inhaled particles to penetrate further into the lung thereby increasing the probability of deposition by diffusion and sedimentation.

The nose, owing to its large internal surface area and the high linear velocity of airflow in the nasal passages even during quiet breathing, is a very efficient first line of defence in protection against dusts and infectious organisms. Impaction against the sides of the nasal chamber owing to turbulence and sudden changes in direction of airflow make it a more efficient filter than the mouth for large particles. During moderate to severe exercise this line of defence is usually lost owing to mouth breathing, thus increasing the probability of particles penetrating to the respiratory tract.

The anatomy of the lung and upper airways determines to a large degree the site and extent of deposition of inhaled particles. The human lung may be visualised as consisting of two zones: the region from the nose or mouth to the terminal bronchioles, termed the conductive zone and the region from the respiratory bronchioles to the alveoli, termed the respiratory or gas exchange zone. The conductive zone or bronchial tree consists of a system of continuously branching airways of rapidly decreasing diameter, whose internal surface is lined with a ciliated epithelium and mucous layer which provides the means for clearance of deposited matter. The respiratory zone consists predominantly of alveolated airways, which do not decrease significantly in diameter towards the periphery. However, because of the successive branching the total cross sectional area and volume of this zone is very large. Table I, taken from the regular dichotomy model of Weibel (1963) demonstrates this clearly and shows that most of the lung volume is contained in the last few millimetres of this branching system.

This anatomical arrangement appears to be a functional adaptation to minimise dead space and resistance to flow in the conductive zone, while maintaining an optimum configuration for the diffusion of gases. However it also acts as an important protective device for the deeper regions of the lung by filtering out the larger inhaled particles before they can reach the alveoli.

An abnormality in this ordered arrangement is likely to increase the overall deposition of inhaled particles. For example, narrowing of the bronchi and bronchioles (generation 0 - 16 in Table I) will increase deposition by impaction. However, destruction of the zone peripheral to the terminal bronchioles, i.e. emphysema, may increase the dimensions of these airways sufficiently to disrupt the passage of air and particles into the alveoli. The focal emphysema characteristic of coalworkers' simple pneumoconiosis, consists of a dilatation of the respiratory bronchioles and may therefore interfere with the normal process of dust deposition.

Once dust has been deposited in the respiratory system there are several ways in which it may be removed from the surface of the airways. If it deposits in the bronchial tree the action of the cilia and mucous sheath lining this region will carry it upwards to the pharynx where it is swallowed or expectorated within hours of being inhaled. Dust deposited beyond the ciliated zone is removed by a different mechanism. The majority is ingested by alveolar macrophages and transported to the ciliary escalator, but some penetrates the alveolarwall where it is either carried to the lymph nodes or remains in sequestered form in the lung tissue. Here it may give rise to a tissue reaction, e.g. silica, or may excite no reaction, as in the case of tin. Soluble substances will be passed in solution into the blood stream or become bound to the lung substance. These latter clearance mechanisms are operative during the course of several months following a dust inhalation and under normal circumstances about 99% of the dust load is cleared. a reduction in clearance efficiency to only 98% therefore results in double the dust load retained. Excessive accumulation of dust may be due to a deficiency in alveolar clearance, which may be a result of an intrinsic deficiency of the clearance mechanism, an excessive inhaled dust load, or both. The production of pneumoconiosis is is likely to be dependent to a large extent on the efficiency of alveolar clearance of dust deposits.

In the causation of pneumoconiosis only dust particles of a certain size are important. Particles greater than 5μ in diameter have a high probability of depositing in the upper respiratory tract and it is the particles smaller than this, the so-called respirable fraction, which are able to penetrate as far as the alveoli in significant numbers. Based on this fact the British Medical Research Council (1943) suggested that measurements of dust concentration should be limited to particles below 5μ, so that sampling instruments as far as possible should duplicate the action of the respiratory system. This is borne out by the fact that dust found in the lungs of coalminers is mostly less than 2μ in diameter and the size for maximum alveolar deposition of inhaled dust is probably between 1 and 2μ. The mass of dust in the lungs of miners examined post mortem correlates well with the category of pneumoconiosis (Rivers et al, 1960) and a method of collection of respirable airborne dust is now employed, based on size selective samples from which mass concentrations can be calculated. Thus only the fraction of airborne dust which is inhaled beyond the terminal bronchioles, i.e. predominantly particles $<5\mu$ diameter, is actually sampled and this is now generally believed to provide the information which is of greatest interest in the evaluation of occupational dust exposure.

CHAPTER 2

HISTORICAL REVIEW

It had been recognised for many years that coalworkers contracted lung disease from inhalation of coal mine dust, although it was not fully established until 1942 by Hart and Aslett that coal dust by itself could give rise to a recognisable disease process. Until that time it was believed that silica in miners' lungs produced silicosis, which was modified by the accummulation of coal-dust. A detailed pathological description of this condition was published by Cummins and Sladden in 1920. However, Collis and Gilchrist (1928) had shown that coaltrimmers, working in the holds of ships and exposed only to coal-dust, developed radiological changes identical to those found in coalface workers. Gough (1940) in a pathological study of coaltrimmers proved that coal dust could give rise to a disabling fibrotic lesion, which was identical to that found in underground coalworkers but distinct from the classical silicosis to be found in miners involved in rock drilling.

Simple pneumoconiosis of coalworkers is classified into categories by assessment of chest radiograph. The International Labour Office (1958) define a system of classification of pneumoconiosis by radiograph which is the one basically in use today, although with slight modifications (I.L.O. 1970). It divides simple pneumoconiosis into 4 categories, 0 (normal), 1, 2 and 3 which have been further subdivided into a 12 point scale by the National Coal Board (Liddell and May 1966). The radiological picture of simple pneumoconiosis shows a number of small, round opacities whose size and profusion determine the category. The individual opacities are categorised as 'p', 'q' or 'r' depending on whether they lie between 0 - 1.5 mm, 1.5 - 3mm or 3 - 10 mm in diameter respectively. Although each category represents a distinct pathological process each stage may progress into the next if the worker continues to be exposed to airborne coal-dust.

Simple pneumoconiosis may change to a more severe stage called progressive massive fibrosis (PMF) which is recognised radiologically by the appearance of massive shadows on the lung fields ($>$ 1 cm in diameter). This stage can progress without further exposure to coal-dust and can be rapidly disabling. PMF is categorised as A,B or C depending on the number, size and extent of large opacities on the lung field against the background of small opacities.

The aetiology of simple pneumoconiosis has been well established. Jácobsen et al (1971) have shown that the mass concentration of the respirable fraction of the airborne dust is the dominant factor in determining the prevalence and severity of pneumoconiosis in coal-workers and that this alone rather than particle count or rank of coal can explain the higher incidence of pneumoconiosis in high rank compared with low rank pits. Rivers et al (1960) demonstrated a clear relationship between the mass of dust in the lungs and the radiological category of pneumoconiosis. A further study (Rossiter et al, 1967) showed that the mineral content, particularly iron, correlated well with the radiological score, because of its greater opacity to X-rays. However, the role of mineral matter and especially quartz in the prevalence and severity of pneumoconiosis has not yet been finally established.

Very little is known, however, of the relative importance of the factors concerned in the development of pneumoconiosis by an individual miner. Lehmann (1935) in an early study found that by passing a dust, average size between 0.5 and 2μ, through the nasal chamber and out through a mouth tube, 63% of healthy miners had a retention efficiency of over 40%, while only 21% of silicotics had, and of these 18% were habitual mouth breathers. It was concluded that poor nasal efficiency in silicotics contributed to their susceptibility to silicosis since the nose provided such an important first line of defence in dust filtration.

Of the physiological factors affecting the amount of dust entering and depositing in the alveolar regions the minute volume of an individual miner will determine the total amount of dust inhaled into the lung. Hadden et al (1967) demonstrated the wide individual variations in minute ventilation between different occupational groups underground and also differences between workers of different ages and physique engaged in similar occupations. If high minute volumes coincide with periods of high dust concentrations

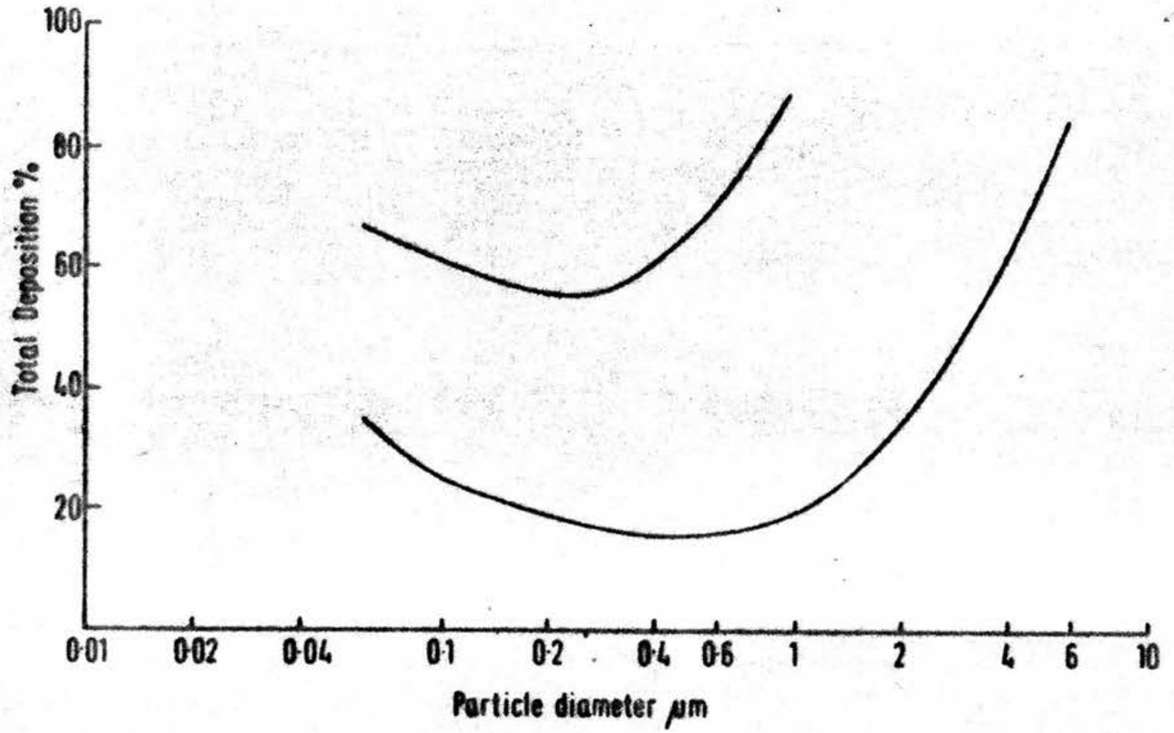

Fig.2 Variation in total deposition of aerosol related to particle size range of published values, adapted from Davies (1964). Variations are due to method of measurement, substance used and its density, tidal volume and breathing frequency of subject and whether nose or mouth breathing was used.

this will increase the amount of dust inhaled for some subjects but not so much for others.

For a given minute volume the quantity of dust deposited is also influenced by the relationship between the tidal volume and breathing frequency. An increased tidal volume and a decreased breathing frequency allow the inhaled particles to penetrate further and spend longer in the lung, thus enhancing the probability of deposition of these particles in the peripheral airways and alveoli. The calculations of Landahl (1950, 1963) and Beeckmans (1965) and the experimental studies of Wilson and La Mer (1948), Landahl et al (1951), Altshuler et al (1957), Dautrebande et al (1957) and Muir and Davies (1967) have demonstrated the importance that individual breathing patterns can play in the degree of dust deposition.

Further measurements of dust deposition in the human respiratory tract have been made by Drinker et al, 1928; Brown et al, 1931; Van Wijk and Patterson, 1940; Landahl and Hermann, 1948; Dennis, 1961 and Dautrebande et al, 1961. These and other studies, which employed several experimental techniques and test dusts, established values of fractional deposition for different sizes of particles, which varied considerably in magnitude (Fig.2).

Individual variation in the percentage of inhaled dust deposited in the lung was first noted by Landahl et al (1951) and subsequently by Altshuler et al (1957) and Muir (1966). Those subjects exhibiting high deposition at one particle size and breathing patterns invariably showed the same characteristics at other sizes and breathing patterns also.

The effects of chronic obstructive lung disease on the deposition of inhaled dusts have only recently been studied. Muir (1970) investigated the behaviour of inhaled particles 0.5µ in diameter during the course of a single breath in asthmatics and bronchitics and observed that only about 50% of the particles inhaled were recovered in the subsequent exhalation compared with 80% in normal subjects. Palmes et al (1971) studied the persistence time of similar particles in the lungs of bronchitic and emphysematous patients during breath-holding. They observed a considerable increase in some subjects, presumably because of the increased dimensions of the air spaces beyond the conducting airways.

The regional pattern of dust deposition in the lung, which it is not possible to measure directly, probably plays an important part in the pathogenesis of pneumoconiosis. Calculations of regional deposition have been made by Findeisen (1935), Landahl (1950, 1963) and Beeckmans (1965) and some indirect experimental studies have been published. Wilson and La Mer (1948) used a radioactive tracer in order to measure directly the amount of material deposited in the peripheral zone of the lungs, and Brown et al (1950) and Altshuler et al (1957) estimated alveolar deposition in the upper and lower tracts by measuring the concentrations of CO_2 and of aerosol in expired air. These studies indicated that maximum alveolar deposition was most likely to occur for particles between 1μ and 3μ diameter. Measurements of regional deposition in a large number of individual subjects have recently been made (Lippmann et al, 1971) with monodisperse radioactively labelled particles between 2 and 12.5 microns unit density diameter (These included non-smoking and smoking normal subjects and both bronchitic and asthmatic patients). They concluded that deposition for particles of this size was primarily due to impaction in the tracheo-bronchial tree although for particles of the order of 2μ diameter sedimentation produces significant deposition in this region. However, there were wide individual variations in tracheo - bronchial deposition for a given particle size - probably because of difference in airway diameters. Alveolar deposition fell rapidly for particles larger than 5μ diameter but did not change appreciably between 2 and 5μ. Tracheo-bronchial deposition was higher in smokers and very much higher in one asthmatic and six bronchitics and alveolar deposition was consequently reduced in these two groups. Bronchoconstriction found in cigarette smokers and bronchitics therefore tends to produce a proximal shift in the deposition pattern of inhaled particles.

Another vital factor connected with an individual's susceptibility to pneumoconiosis relates to the efficiency of clearance of deposited dust from the alveoli. Many investigations have been made into the rate of clearance of deposited matter from the respiratory tract and in coal miners probably about 99% of dust deposited during a lifetime's exposure is cleared (Policard 1960). However individual studies are rare and, although investigations on individual rates of tracheobronchial clearance have been made on human subjects (Albert et al (1969), Camner and Philipson (1971)) this only represents the fate of inhaled particles during the first few hours post-exposure and does not provide information about the long term fate of inhaled dust which has deposited in the alveolar regions. Individual variations in the rate of alveolar clearance and the tissue reaction to deposited dust have not been studied, but the latter presents severe practical problems in human subjects.

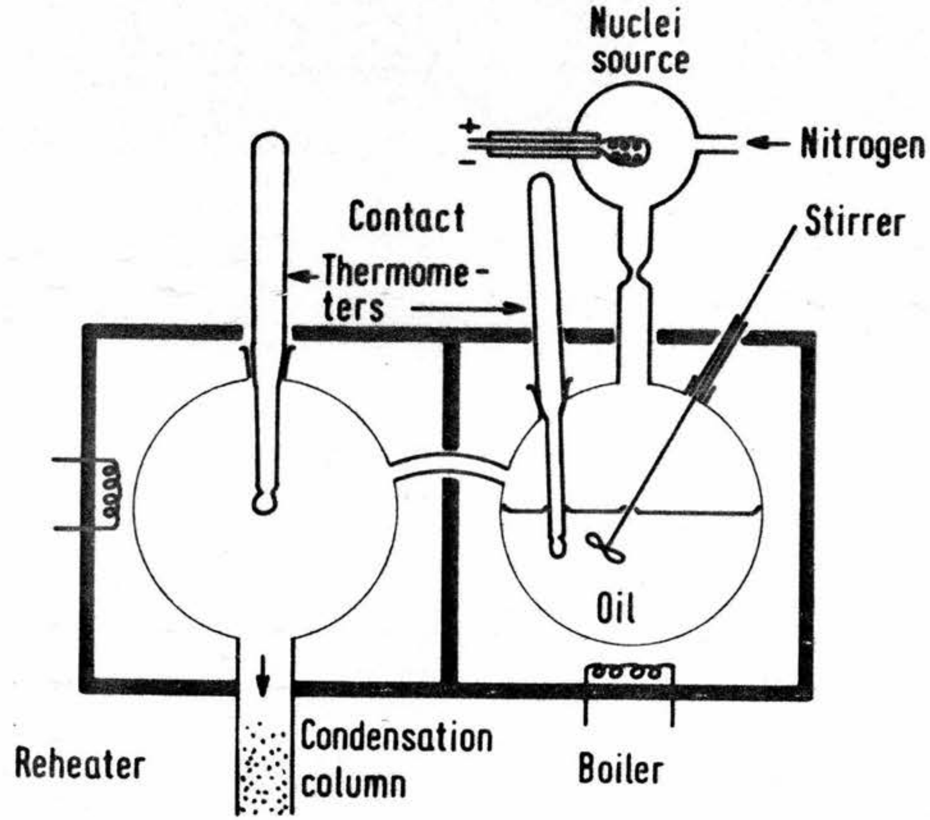

Fig. 3 Modified La Mer-Sinclair aerosol generator

CHAPTER 3

EXPERIMENTAL APPARATUS AND PROCEDURE

Most airborne dusts produced during the course of an industrial process consist of particles whose size range is very wide, often varying from submicronic to almost 1 mm in diameter in the same dust cloud. However, as mentioned in Chapter 2, only particles less than about 5µ in diameter have a substantial probability of penetrating as far as the alveoli. For experimental purposes it is easier to study the behaviour of monodisperse particles rather than to study the behaviour of a mixed dust cloud. In this work an experimental monodisperse cloud of 1µ diameter particles has been used to study the variations in percentage deposition of aerosols in the lungs of coalworkers with and without simple pneumoconiosis

3.1 Aerosol Generator

The generator used for production of monodisperse aerosols was a modified version of the apparatus described by Muir (1965) (Fig.3). His apparatus was itself a modification of a generator first designed by La Mer and Sinclair (1943), in which the vapour of a heated liquid was allowed to mix with and condense on a controlled concentration of nuclei. Muir's modification incorporated an inverted cooling tower (after a suggestion by Wooding (1953)) thus reducing convection currents which interfered with the monodispersity of the aerosol.

In the present study the generator has been adapted for production of aerosols in the range 0.25 - 1.5µ diameter. Particles of approximately 1µ mean diameter have been used throughout this series of experiments. The substance used was di-2-ethylhexyl sebacate, an inert, non-toxic oil of low vapour pressure (used in the manufacture of food containers) which withstands continuous heating without decomposition, is insoluble in water and has only one isomer. It is therefore very suitable for use in inhalation experiments.

The oil was heated in a 2 l flask, through which a stream of nitrogen passed at 0.75 l/min. A heated nichrome wire coil coated with sodium chloride provided a steady concentration of condensation nuclei. The nichrome wire was coated as thickly as possible with sodium chloride by allowing the fumes from fused sodium chloride to deposit on it.

By means of a transformer, a current of 3.25 amps to the element heated it to just below dull red-heat, under which conditions the supply of nuclei lasted for at least 24 hours. Between each coating the element was washed in distilled water and dried, otherwise no further precautions needed to be taken to ensure a regular concentration (about 10^6 particles/cc) of spherical nuclei 0.02 - 0.08μ in diameter (Swift (1967)).

Vapour and nuclei passed into a second flask through a jet to facilitate mixing, and were reheated to 250°C before passing down the cooling column where the vapour condensed on the nuclei to produce an approximately monodisperse aerosol. It has been established (Muir 1965) that radial inhomogeneity of particles across the tube, caused possibly by condensation on the walls, can be diminished by a slower flow rate and by positioning a glass cone centrally in the tube. This adaptation was employed in this generator which allowed aerosol to condense in the space between the glass cone and the walls of the tube. Samples were extracted by a 150ml syringe at intervals during the experiment, in order that a constant check on the size and uniformity of the aerosol could be maintained. By raising the temperature of the oil in the first flask the particle size of the aerosol could be increased, the temperature being maintained to within an accuracy of $\pm$ 0.1°C by a mercury contact thermometer.

3.2 Uniformity and mean particle size of aerosols

An assessment of the uniformity of particle size of aerosols from the modified La Mer-Sinclair generator was carried out by Muir (1966) on this apparatus using samples collected on cover slips in a thermal precipitator (Watson, 1936). From these measurements it was clear that particles in any given aerosol cloud between 0.3μ and 0.9μ diameter were distributed in an approximately log-normal manner with a geometric standard deviation of about 1.13. This method is suitable for particles up to 5μ median diameter although other workers have reported that the aerosol becomes more uniform as the particle size increases. Uniformity is important when the concentration of aerosols of small diameter is measured by optical means, because the presence of a few larger particles would cause scattering of a disproportionate amount of light. However, this ceased to be a serious problem when dealing with particles of approximately 1μ diameter.

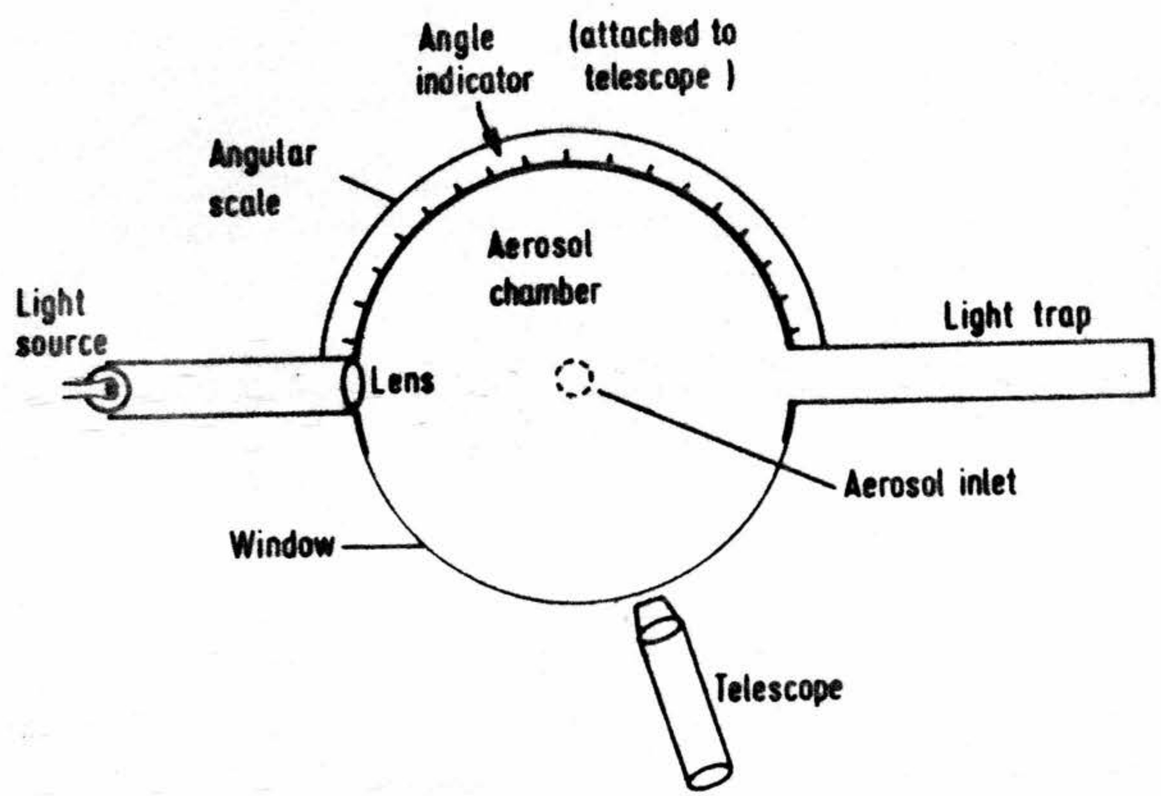

Fig. 4 Sectional view of the 'Owl', for measuring particle diameter of aerosol

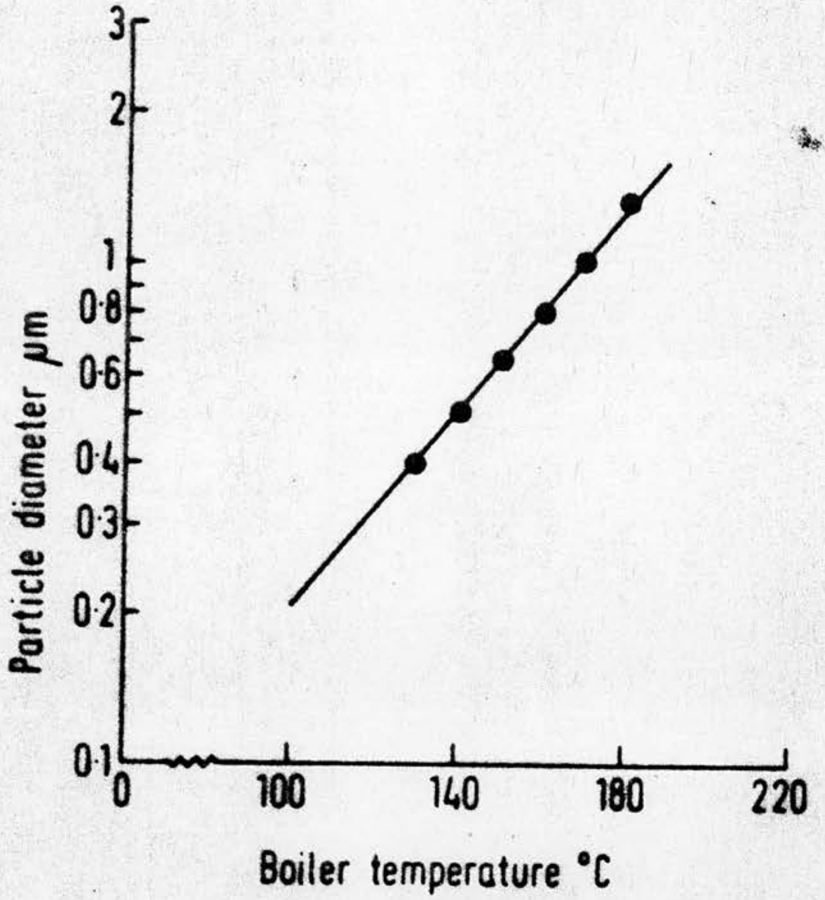

Fig. 5 Effect of boiler temperature on particle diameter for La Mer-Sinclair Generator at a nitrogen flow of 0.75L/min (Reheater temperature = 250°C)

Each point represents the mean of four measurements. The line is the best fit by eye.

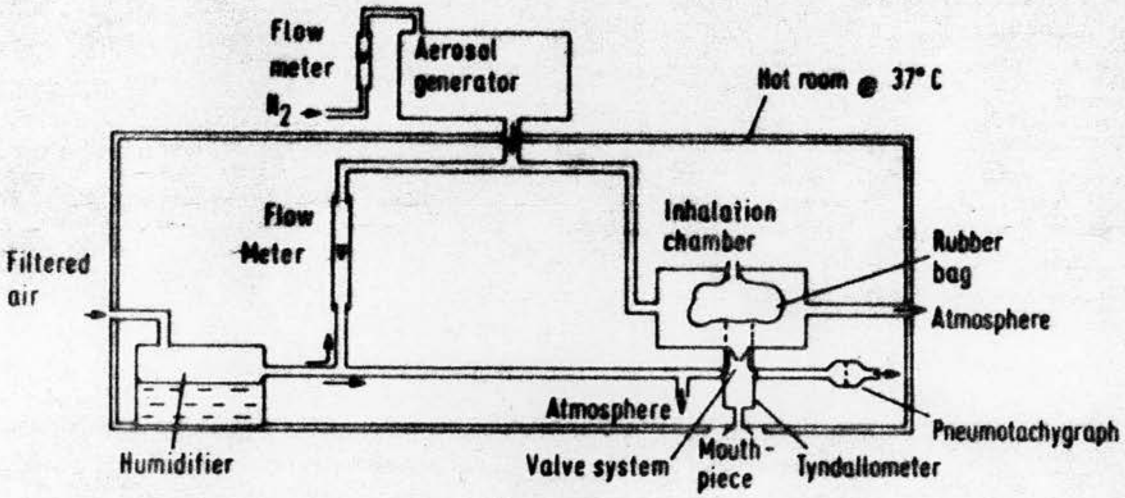

Fig. 6 **Diagram of Aerosol supply system and inhalation apparatus**

Once the boiler had been set at the required temperature for production of 1μ diameter particles, samples were extracted from the condensation column and their size was checked using a method developed by La Mer and Sinclair (1943). The measuring apparatus, called the "Owl", consisted of a flat cylindrical chamber with an inlet and outlet for aerosol and a perspex window round a third of its circumference, through which a rotating telescope could be focused (Fig.4). When aerosol was introduced into the chamber and a parallel beam of white light shone through it, a series of spectral colours could be seen through the telescope at an angle to the beam (The Tyndall Effect). The angles at which the colours appeared and their sequence depended on the mean size of the particles present.

In this apparatus a 12V 100W lamp was used to produce the beam, which passed through the blackened chamber into a light trap. The telescope was rotated until the first red colour was observed and the angle at which it appeared was measured. This was repeated for the red parts of subsequent visible spectra, so that the angles at which the various red colours appeared could be read off a series of curves plotted by Sinclair (1950, page 84), in order to obtain the approximate size of the suspended particles. Repeated use of the "Owl", while the generator was running provided a rapid method of monitoring the particle size and also gave an indication of fluctuations in the concentration and uniformity of aerosol: that is, the brighter the colours, the more homogeneous was the aerosol cloud. By using this method, the relationship between the temperature of the boiler and the size of the particles was established and the results are shown in Fig. 5.

3.3. Inhalation Apparatus

The aerosol passed out of the condensation column and was immediately diluted in a stream of clean filtered air flowing at 40-50 l/min (Fig.6). The diluted aerosol was carried in the air stream to a reservoir of 3.2 litres capacity where complete mixing could take place. The subject was able to inhale from this chamber and any excess aerosol was led off through a tube to the outside of the building. A rubber bag situated inside the chamber was connected to the outside of the chamber by a short tube which allowed air to pass into the bag whenever the subject inhaled thus equilibrating the pressure inside the chamber and maintaining a constant aerosol concentration. Part of the clean air supply provided by means of

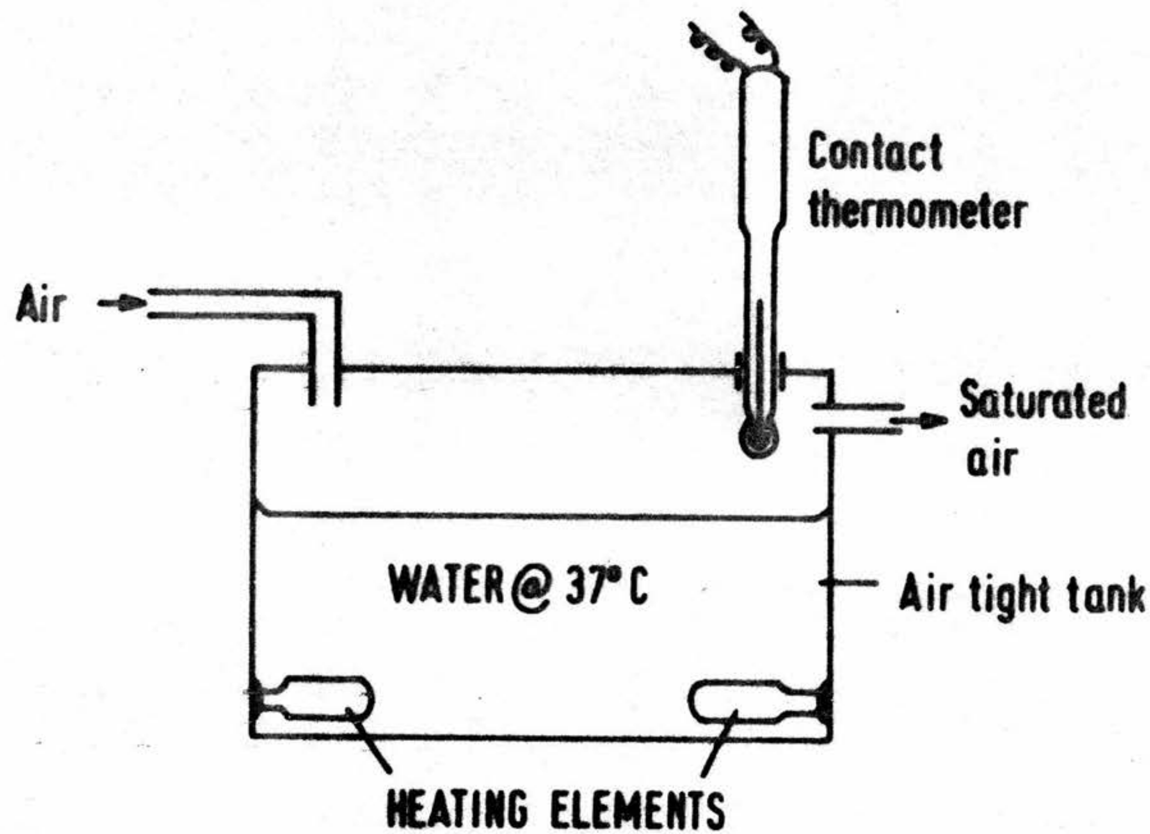

Fig. 7 Inhaled air humidifier

a rotary pump fitted with a filter to remove all particles larger than 0.1µ diameter, was diverted to a second tube from which the subject could inhale, in order to wash out any suspended particles from the lung air.

A 3-way valve system allowed the subject to inhale either aerosol or clean filtered air. The exhaled air passed through an outlet valve to a pneumotachygraph (Fleisch 1925) which measured the expired air flow. The third arm of the valve led to a mouthpiece. The concentration of the aerosol was measured in a Tyndallometer close to the mouth by passing an intense beam of light through a glass window in one side of the assembly. The intensity of the scattered light, which is proportional to the concentration of particles if the aerosol is uniform, was recorded during inspiration and expiration.

The whole experimental apparatus except the aerosol generator and data recorders was housed in a constant temperature hot room made of expanded polystyrene sheeting. The temperature in the room was thermostatically controlled at 37°C, so that both the aerosol and clean air supplies were heated to body temperature. A humidifier was placed in the circuit (Fig.7) so that inspired clean and aerosol-laden air-streams were at least 90% saturated with water vapour at 37°C when measured at the mouthpiece by a wet and dry bulb thermometer method. Since the pneumotachygraph was heated by this method and the Tyndallometer and mouthpiece assembly were addditionally heated by circulating water at 39°C, water vapour could neither condense on the aerosol particles, nor on the inside of the mouth and airways, or in the Tyndallometer or pneumotachygraph.

Since all the inspired and expired airstreams were heated to body temperature and saturated with water vapour no volumetric corrrections were necessary for the aerosol concentration readings. Muir and Davies (1967) showed that results of aerosol deposition experiments did not differ significantly under such conditions compared with those obtained when air was breathed at room temperature.

3.4 The Valve and tap assembly

The 3-way valve system is illustrated in Fig. 8. It consisted of a conventional aluminium 3-way tap adapted so that it could be turned by means of an air-driven solenoid switch. The valve was turned in the barrel almost instantaneously with a differential pressure of 10 p.s.i. which could be reversed by changing the direction of the air pressure

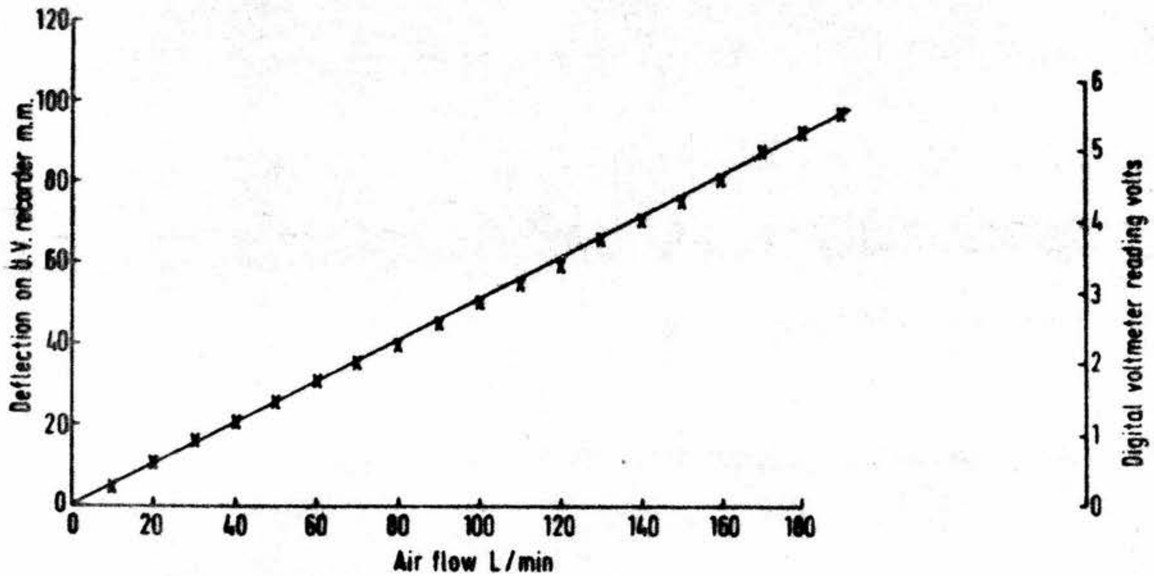

Fig. 9 **Relationship of galvanometer deflection on U.V. recorder and digital voltmeter reading to step changes of airflow through the pneumotachygraph.**

Each point represents the mean of two to four measurements.

The line is the best fit by eye.

in the switch. In this way the subject could be made to inspire aerosol or clean filtered air from the aerosol inhalation chamber or clean air supply. The expired air was prevented from flowing back up these inlets by means of light spring-loaded poppet valves made of mica discs which formed an efficient seal in the aluminium seating of each inlet tube.

A single exhalation port was used whether the subject inspired aerosol or clean air. It passed out at right angles to the inlet tubes through another one-way poppet valve. The third arm of the valve system led through an aluminium block which formed the Tyndallometer, to a short mouthpiece. The effective dead space of the valves and rotating tap was measured by filling it with water and was found to be 50 ± 1 cc.

3.5 The measurement of expired air flow

The expired air passed through a standard pneumotachygraph (Fleisch, 1925) which monitored the change in pressure across a thin metal mesh. The drop in pressure across this obstruction is directly proportional to the airflow and two pressure tubes led from either side of it to a differential pressure transducer (Mercury Electronics Greer Micromanometer, type M3, Capsule type A10) which registered the pressure change in mm H_2O. This was converted into an electrical signal which could either be displayed on a U.V. recorder or reproduced in digital form on punched paper tape with no further amplification.

The pneumotachygraph was calibrated and its linearity determined by passing a series of known steady flows through it covering the range encountered during breathing at rest and moderate exercise, i.e. 0 - 200 litres/minute. Air from a domestic vacuum cleaner was passed through two 0 - 100 litres/minute flow meters (Rotameter Manufacturing Co. Ltd.) placed in parallel. Adjustment of a tap upstream of the flow meters allowed the flow to be increased or decreased in steps of 10 litres/minute. The output of the pressure transducer was displayed on a U. V. recorder and also on a digital voltmeter for each step change in flow. The results are plotted graphically in Fig.9, which demonstrates the linearity of the flow measuring system. The accuracy of the flow meter was checked by passing a steady flow through it into a dry gas meter over a timed interval. An average volume of 40 litres per minute through the gas meter corresponded exactly with a steady flow of 40 litres/min in the flow meter at ambient temperature.

The volume of each breath, which was normally calculated from the data on the punched tape by integration of the voltage readings during expiration was also integrated manually from the U.V. record by the method of Simpson's Rule. This procedure was carried out on seven consecutive breaths which passed through the pneumotachygraph into a dry gas meter. The average volume per breath was calculated by dividing the total meter reading by the number of breaths,

i.e. $\frac{\text{Meter reading}}{\text{No. of breaths}} = \frac{10.83}{7} = 1.55$ litres per breath.

Applying Simpson's Rule to the U.V. record of flow in centimetres the area under the curve,

$$A = \frac{h}{3}\left[f_o + f_n + 4\ (\text{odd ordinates}) + 2\ (\text{even ordinates})\right] \times C$$

where h = time interval between ordinates = 0.1 sec.

f_o = first ordinate

f_n = last ordinate

C = conversion factor = slope of graph of flow (in litres/sec) against U.V. recorder deflection (in centimetres) = 0.317

Average area = 1.63 litres per breath.

The difference between the two methods is 0.08 litres, which is about 5% of the total volume per breath. Since the absolute volume is not required in the calculation but is only necessary for standardisation of the deposition rate for each subject, this difference is considered small enough to be neglected.

3.6 Measurement of Aerosol Concentration

The concentration of aerosol during inspiration and expiration was measured by means of a Tyndallometer, which was situated close to the mouth between mouthpiece and the 3-way tap (Fig.8). It consisted of a $1\frac{1}{2}$" cubical aluminium block with a cylindrical hole bored through each plane, one of which led to the mouthpiece, one allowed a light beam to pass through to a light trap and the third led to a photomultiplier.

Light reflected by the aerosol particles at right angles to the beam passed through this window into the photomultiplier. In order to prevent as much internal reflection of the beam as possible the inside of the Tyndallometer was painted matt black and coated with fine carbon particles by holding it over burning camphor. Since the inlet window for the light beam caused most of the internal reflection, a series of diaphragms were positioned between it and the centre of the Tyndallometer to concentrate the beam as far into the centre of the block as possible. Diaphragms were also placed inside the window leading to the photomultiplier. These precautions resulted in a background scatter from the Tyndallometer of only 2 - 3% of the total signal when 1μ diameter aerosol particles were present at the concentration found during inspiration from the inhalation chamber. Channels were drilled in the Tyndallometer so that water at 39°C could circulate through it thus preventing condensation of water vapour from the expired air.

The source of the light beam to the Tyndallometer was a 12V 100W tungsten iodide quartz projector lamp. The lamp was fixed at one end of an optical bench and the beam was focused by means of a plano-convex lens, a diaphragm and a biconvex lens, so that a nearly parallel beam of light passed into the Tyndallometer fixed at the opposite end of the bench. The lenses were so placed that the brightest part of the beam was at the centre of the Tyndallometer, that is, where most of the light reflected from the airborne particles would be recorded by the photomultiplier. The diameter of the beam at this point was about 5 mm.

To reduce any fluctuations in the intensity of the light source with alternating mains frequency a D.C. mains rectifier was placed in the power circuit.

3.7 The Photomultiplier

The photomultiplier consisted of a 50 mm nominal diameter tube with 13 venetian blind type dynodes (Electrical and Musical Industries Ltd., Type 9501B). The high voltage to the cathode was supplied by a feed back oscillator with rectifier (Isotope Developments

EHT Unit Type 532/D) and under normal circumstances input ranged from 810 - 860 Volts for full scale deflection, i.e. with full inspired concentration of aerosol. A fixed integrated circuit amplifier was connected to the output of the photomultiplier, such that full scale deflection on the display of the digital voltmeter (10 volts) was produced by an input of not greater than 10 μA, which is the maximum allowable anode current through the photomultiplier circuit, under D.C. conditions. In practice 4 μA input to the photomultiplier gave a voltmeter reading of 8 volts.

3.8 The recording system

The outputs of the photomultiplier and of the differential manometer (monitoring pressure changes in the pneumotachygraph) were displayed in two ways. Firstly, the voltage outputs during recording were each sampled approximately ten times per second, the photomultiplier output followed by the manometer output being sampled and stored in an electronic data logging circuit.* The stored voltage readings (three significant figures up to a maximum of 9.99 volts) were then released, converted from analogue to digital form and displayed on a digital voltmeter (Solartron Electronics Group Type LM 14202). A Binary Coded Decimal Fan Out Unit (Type EX 1418) fixed to the back of the voltmeter carried out the analogue to digital conversion.

The voltmeter was operational over a 0 - 20 volt range and had a 20m V sensitivity within this range. When it was switched to the automatic mode, the individual outputs of the photomultiplier or manometer were scanned 33 times per second and could be displayed by moving a switch on the data logger to the required position. In this way the aerosol concentration or airflow could be inspected during any part of the respiratory cycle.

With the voltmeter set to the manual sample mode the photomultiplier and manometer outputs, which were sampled and stored every 0.1 second, were scanned and displayed alternately by the voltmeter. The output of the voltmeter was recorded on a paper-tape punch (Westrex Teletype 110), in the order (1) Photomultiplier readings (2) Manometer readings.

The punch used tape one inch wide and an eight hole even parity code, which was printed out in straight binary form at a maximum operating speed of 110 characters per second. The normal operating speed utilised

* Faul - Coradi (Scotland) Ltd.

ing page 19

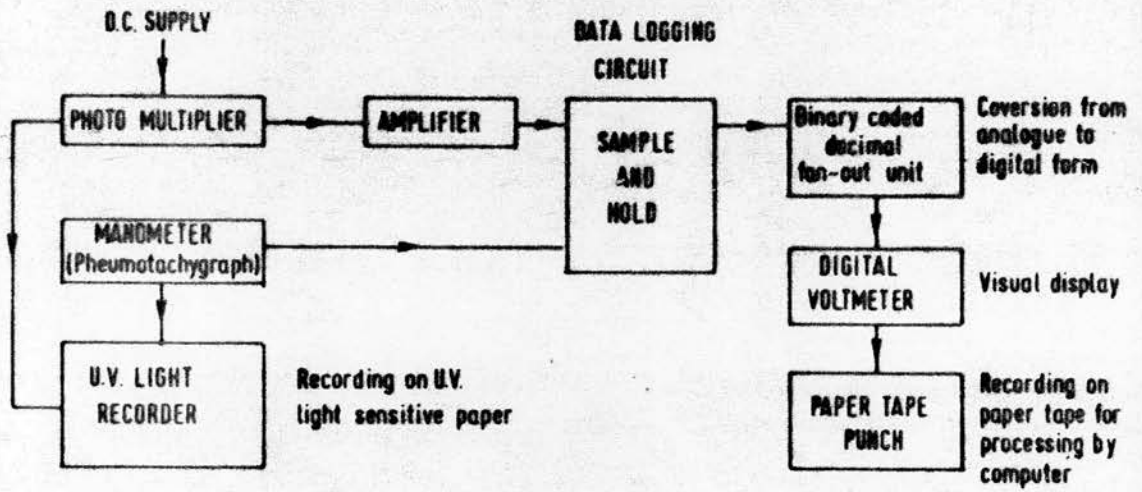

Fig. 10 Diagrammatic representation of recording system.

was 66 characters per second, since the photomultiplier and manometer readings (three digits each) were read 11 times each second.

The second method of recording employed an ultra-violet light S.E. 2005 recorder (S.E. Laboratories Ltd., Middlesex, England). The outputs of the photomultiplier and the differential manometer were displayed on U.V. light sensitive paper for the first 5 or 6 breaths during steady state breathing at each work level. A visual record was thus obtained for each subject so that any fault in the experiment was immediately recognisable. The shape of the expired aerosol concentration curve could readily be observed. The recording system is illustrated diagramatically in Fig. 10.

CHAPTER 4

M E T H O D S

4.1 Experimental Procedure

The subject, who sat on a constant load bicycle ergometer, wore a nose-clip and breathed clean filtered air through the mouthpiece for one minute or as long as was required for the signal on the U.V. recorder and digital voltmeter to register a zero reading during inspiration and expiration. At this point all airborne particles were considered to have been eliminated from the lung air. He breathed in time to a voice on a tape recorder, which gave the commands "IN" and "OUT" alternately at two seconds intervals. A series of one to three characters were punched on the paper tape in order to identify the subject followed by the zero aerosol concentration signal during inspiration. At the end of a normal expiration the subject was switched into the aerosol supply. At this point recording started and continuous measurements of aerosol concentration and airflow were made during the subsequent twenty breaths at rest. After the twentieth breath the switch was returned to the clean air position and the subject began pedalling the bicycle at a work load of 100 kgm/min, whilst maintaining his breathing rate at 15 breaths per minute. Three minutes were allowed for the subject's ventilation to reach the steady state. The subject code and zero aerosol concentration were punched on to the tape and after a normal expiration twenty breaths were again recorded. This procedure was repeated at work loads of 300 and 500 kgm/min. A work load of 700 kgm/min was used for some of the earlier subjects but they found it difficult to maintain a breathing rate of 15 breaths per minute at this workload.

All smokers refrained from smoking during the course of the experiments and for at least an hour beforehand where possible.

Lung function studies were carried out on each subject either before or after the aerosol deposition measurements. Measurements of FEV_1 and FVC were made using a modified Gaensler spirometer. Four readings were taken, the first was discarded and the subsequent three were averaged.

The vital capacity and its subdivisions, inspiratory capacity and expiratory reserve volume, functional residual capacity, residual volume, total lung capacity and single breath carbon monoxide transfer factor were measured using the Meade, Saunders Resparameter (P.K. Morgan Ltd., Chatham, Kent). Age, height, sitting height and body weight were also recorded.

Six months after the original lung function measurements were made a direct writing spirometer became available. From the continuous record of volume against time measurements of flow at low lung volumes were possible. FEV_1 and FVC were also measured on this occasion from the volume-time recorder (Vitalograph : Garthur Ltd.) Maximum expiratory flows at 50% VC ($MEF_{50\%}$) and from 50 - 75% VC ($MMEF_{50-75\%}$) were determined from this record for 51 of the original group of 58 subjects. No significant differences in FEV_1 and FVC measured on the two occasions was found.

Each subject was presented with a series of standard questions about respiratory symptoms and smoking history. The questionnaire used was the shorter version of the National Coal Board's questionnaire developed for use by the Pneumoconiosis Field Research group (Crooke-Morgan et al 1964) and was modified from one originally developed by the Medical Research Council (1961).

4.2 Calculation of Results

The amount of aerosol deposited per breath was determined by means of an ICL 1904 computer and the punched tape record. The amount of aerosol expired was calculated using Simpson's rule by integration of the products of each reading (taken every 0.09 second) of aerosol concentration (C_E) and airflow (F_E) after the zero aerosol concentration and zero airflow readings (recorded during the previous inspiration) had been subtracted from each respective reading ($C_E \cdot F_E$). This calculation gave, in arbitrary units, the amount of aerosol exhaled. The inspired concentration, C_I, was determined from the average of the inspired aerosol concentration readings for each breath.

The volume expired per breath (V_T) was also calculated in arbitrary units by applying Simpson's Rule to the expired flow readings and this was converted to litres by a calibration factor previously determined. The inspired volume was assumed to equal the expired volume and was multiplied by the inspired aerosol concentration, in order to give, in arbitrary units, the number of particles inspired.

An allowance had to be made for the small dead space, V_D, of the mouthpiece assembly (50 cm^3). The first part of each inspiration was considered to contain aerosol at the end tidal concentration (C_T) of the previous expiration and, although it may have been slightly greater than this, the error involved in making this assumption is insignificant for the average tidal volumes used.

The fraction of aerosol deposited (D) in each breath is given by the relationship:

$$D = 1 - \frac{(C_E \cdot F_E)}{C_I \cdot (V_E - V_D) + C_T \cdot V_D}$$

The fractional deposition was averaged for twenty breaths and expressed as a percentage of the average amount inhaled per breath.

In order that the computer could determine when inspiration and expiration took place, the expired flow signal was employed as the indicator of the two phases of the respiratory cycle. Since inspiratory flow was not recorded during the course of the experiment, it had to be assumed that inspiration began and ended at the end and beginning of expiration. Therefore flow during inspiration was recorded as zero, or more normally 0.05 - 0.10 volts above zero to allow for drift, so that any deviation above this level was caused by expiration. In practice expiration was deemed to have started when flow rose to 0.25 volts above zero and to have ended when the flow signal fell below this level. Zero was usually equal to about 0.1 volts so that 0.25 - 0.10 = 0.15 volts represented between 1 and 2% of full scale deflection. This resulted in the under-recording of expiratory flow per breath by a negligible amount.

Although it has been assumed in these calculations that the inhaled and exhaled volumes per breath are equal this is not strictly true if the respiratory exchange ratio is less than unity. During exercise it approaches 1.0 but at rest it may be as low as 0.8. In this case, however, the amount of aerosol expired would be overestimated by a maximum of 0.5%, which is small enough to be neglected.

There may also be a change in mean lung volume from breath to breath, so that the exhaled volume may differ from the inhaled volume during a single respiratory cycle. The mean lung volume must remain constant on average, however, and no significant error is likely to arise if

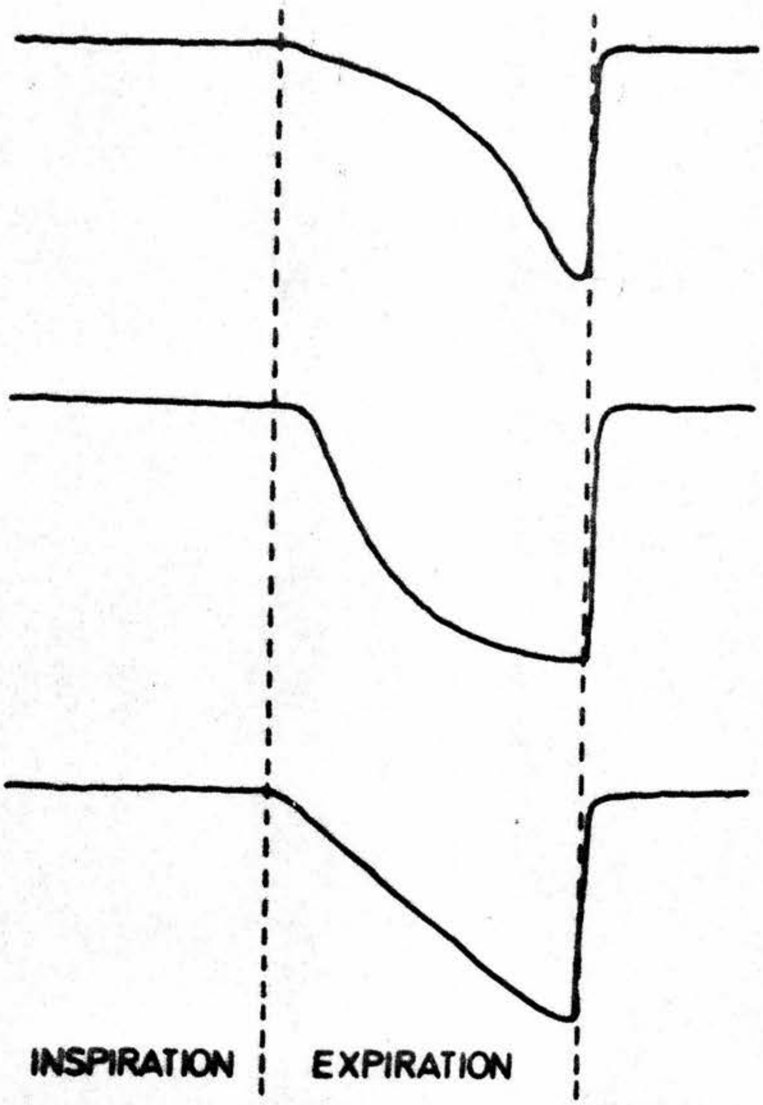

Fig. 11 **Variations in the Shape of the expired aerosol concentration curve during steady state breathing.**

The curves are typical examples of the three curve shapes taken from an ultra-violet light recording (aerosol concentration VS time). Each represents a single breath.

TABLE 2

Anthropometric data, occupational history, smoking habits and aerosol deposition for pneumoconiotic and control miners.

Pneumoconiotics

Subject No.	X-ray cat.	Age (yr.)	Ht. (cm.)	Wt. (kg.)	Years Worked U/G	Years Worked Face	Smokers* (%)	Deposition/ (%)	Shape Factor Convex (% in each group)	Shape Factor Intermediate (% in each group)	Shape Factor Concave (% in each group)
2	1/0	62	177	57	38	32	+	25.3 (0.9)			+
6	1/1	58	172	73	40	6	+	21.8		+	
7	1/2	62	169	88	50	48	x	18.9	+		
9	1/1	55	165	67	42	32	+	23.5		+	
13	0/1	62	172	95	40	40	+	26.5			+
15	2/2	51	175	91	36	20	x	20.2		+	
16	1/1	52	170	77	38	30	+	15.9	+		
22	1/1	62	161	68	28	28	+	27.6			+
23	2/1	62	169	91	46	20	x	21.0		+	
25	1/1	56	155	59	42	42	+	22.9		+	
29	1/1	64	173	74	49	35	–	24.3			+
32	1/1	50	175	93	34	25	+	17.9	+		
34	2/1	64	175	70	51	51	+	21.9		+	
42	1/1	54	172	76	40	29	+	22.3		+	
44	1/0	60	165	73	45	40	+	17.5		+	
45	2/2	56	164	75	42	42	+	18.3 (1.0)		+	
48	1/1	63	164	64	49	41	x	25.3			+
52	0/1	58	169	78	44	36	+	15.3	+		
58	1/1	60	170	69	47	32	+	18.3		+	
Mean		58.5	169.1	75.7	42.2	33.1	74	21.3	21	53	26
S.D.		4.5	5.6	11.3	5.9	10.7	–	3.6	–	–	–

Controls/

TABLE 2 (contd.)

Subject No.	All o/o	Age (yr.)	Ht. (cm.)	Wt. (kg.)	Years Worked U/G	Years Worked Face	Smo-kers* (%)	Depos-ition⧸ (%)	Shape Factor: Convex (% in each group)	Shape Factor: Intermediate	Shape Factor: Concave
1		66	164	79	46	30	x	21.0	+		
3		55	175	79	41	42	–	22.6	+		
4		63	165	65	50	40	+	19.0	+		
5		61	171	73	48	35	+	19.2	+		
10		53	163	79	39	39	+	20.6		+	
11		61	170	71	45	45	x	15.7		+	
12		64	166	57	49	49	x	17.6	+		
14		55	186	69	40	40	+	21.2		+	
18		48	172	78	20	14	+	24.0		+	
19		53	163	69	40	38	+	25.6			+
20		62	163	78	46	46	–	16.4	+		
21		62	175	78	49	48	+	21.0		+	
24		59	156	45	45	44	+	25.0			+
26		61	168	71	47	4	+	17.2		+	
27		55	164	69	42	5	–	23.1			+
28		63	167	69	37	37	+	22.9		+	
30		61	160	63	43	37	+	19.9		+	
31		62	164	84	45	40	–	17.0	+		
33		64	163	78	51	50	+	22.0		+	
35		60	160	70	47	43	+	22.2		+	
36		62	164	67	47	47	+	18.7		+	
37		63	174	62	49	49	+	14.9	+		
38		60	171	92	41	16	+	21.0	+		
39		62	163	62	12	12	+	17.6 (0.9)	+		
40		62	161	65	48	36	+	25.9			+
41		53	174	63	40	40	+	24.8			+
43		57	172	91	40	38	–	14.2	+		
46		55	168	71	42	42	–	14.7	+		
47		52	158	80	39	38	+	18.8 (1.2)		+	
49		51	170	79	26	26	+	21.3		+	
50		56	175	71	42	42	+	26.2			+
51		52	175	84	36	36	+	18.6	+		
53		52	173	78	38	38	+	23.3			+
54		57	170	90	35	35	–	15.7	+		
55		64	162	66	37	37	+	21.7 (1.9)		+	
56		61	174	58	28	28	+	25.4			+
57		57	159	56	11	11	+	24.1		+	
Mean		58.5	167.7	72.4	40.4	35.8	72	20.8	38	41	22
S.D.		4.4	6.6	10.4	9.5	11.9	–	3.6	–	–	–
P values ⧸		N.S.	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.		N.S.**	

* + = smoker; – = non-smoker; x = ex-smoker. ⧸ Deposition at V_T = 1.6L unless stated

(figures in brackets = V_T in litres) ⧸ 2 sample t test. N.S.= differences between groups not significant. ** = Chi Square Test.

deposition is averaged over twenty breaths.

Examples of recordings of inspired and expired aerosol concentration and expired air flow are shown in Fig. 11. The instantaneous expired aerosol concentration was plotted against expired volume and the resulting curve has been classified according to its general shape (i.e. convex, intermediate or concave). Examples of each are illustrated in Fig. 12.

4.3 Subjects

The experimental subjects were 58 coalworkers selected from the South Scottish coalfield. All men still at work in this area of the coal industry who were known to have been certified as having category 2 simple pneumoconiosis (I.L.O. scale) and who lived within reasonable distance of the laboratory were invited to take part in the study. This group consisted of 36 men of whom 19 were able to take part. The other 17 did not attend owing to illness, recent retirement, or refusal. Another 36 men were selected to act as controls with 36 more as reserves and of this group 39 were able to take part. The control group were drawn from the same pits as the pneumoconiotics and were matched for age and occupational history but were known to have normal X-rays (category 0). The total of 36 subjects initially selected with category 2 pneumoconiosis represented about 0.5% of a total population of 7200 miners distributed amongst 5 pits. This figure is in keeping with the well-known low prevalence of the disease in Scotland (Hicks et al 1961). The details of the subjects are shown in Table 2.

Individual X-rays were mixed and examined by an experienced reader (Dr. S. Rae) who either confirmed or recategorised the original reading. Where subjects had not had a recent X-ray, that is, within the previous 12 - 18 months, fresh X-rays were obtained and examined in the same manner. The final categorisation of the pneumoconiotics was made using the N.C.B. elaboration of the I.L.O. scale and ranged from 0/1 to 2/2. The control group all fell into the group 0/0.

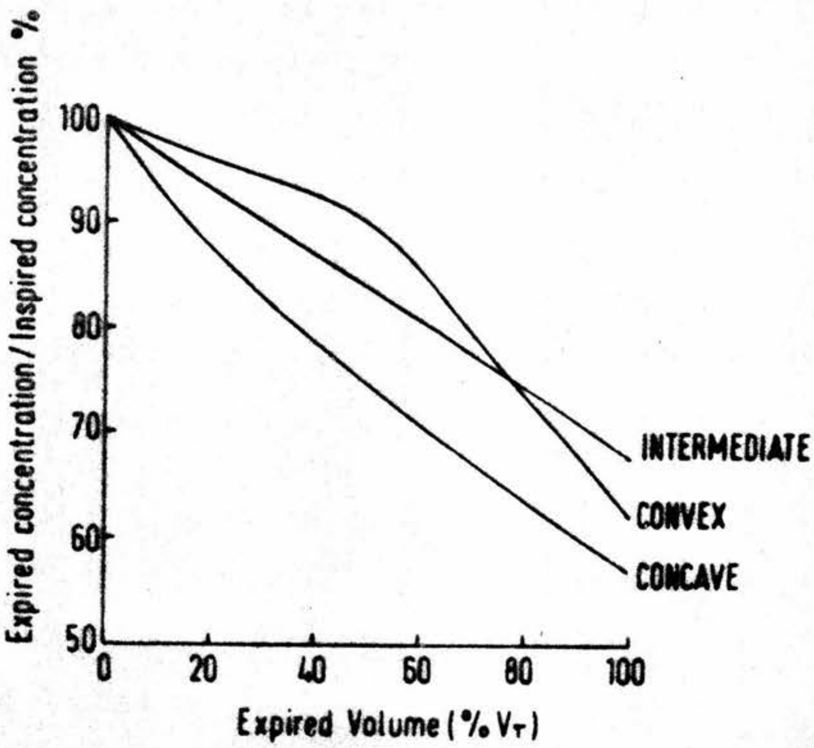

Fig. 13 **Variations in the** shape of the **expired aerosol** concentration curve (Shape Factor) **with respect** to expired volume during **steady state** breathing.

Each curve is derived from the mean of 20 breaths for three typical subjects. 100% on the ordinate and abscissa represents mean inspired aerosol concentration and mean tidal volume respectively.

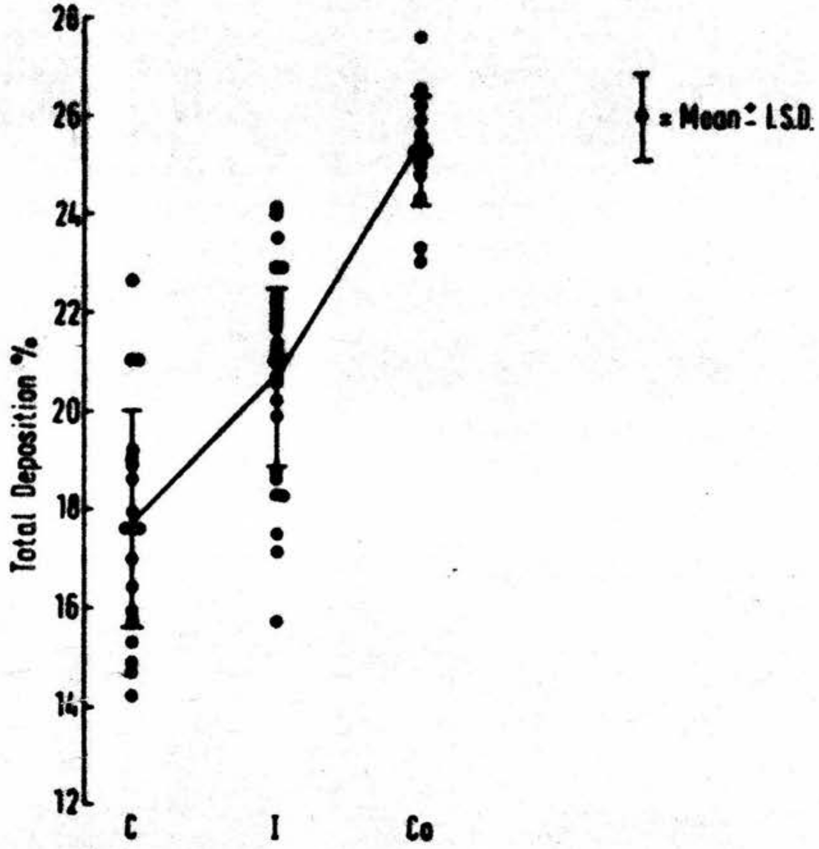

Fig. 14 Relationship between deposition and shape factor.

CHAPTER 5

RESULTS

5.1 Total deposition and shape factor

The average percentage deposition, calculated where possible over 20 breaths at four workloads for each subject, was plotted graphically against tidal volume (B.T.P.S.). Selected examples are shown in Fig. 12. In the majority of cases deposition increased linearly with tidal volume, a few showed little change with tidal volume and in six subjects the deposition appeared to decrease with increasing tidal volumes. The slopes of deposition against tidal volume were calculated by the method of least squares and regression equations were thus obtained for each subject.

Aerosol deposition was standardised for each subject by calculating the deposition from the regression line at a tidal volume of 1.6 litres, which was about the midpoint of the range in most cases. Table 2 shows percentage deposition at this tidal volume for the pneumoconiotic and control groups where sufficient points were available to draw regression lines.

The shape of the expired aerosol concentration curve with respect to volume (Shape Factor) has been classified visually and it was found possible to divide the subjects into three groupings based on the shape of this curve, as follows:

(i) Convex
(ii) Intermediate
(iii) Concave

These are illustrated in Fig. 13.

The variations in the shape factor are also shown for each subject in Table 2.

The relationship between shape factor and aerosol deposition is shown in Fig. 14. Deposition increased on average from 17.6% for subjects with convex curves to 25.2% for those with concave curves. [redacted] For subjects with intermediate and concave shape factors deposition was significantly different from subjects with convex curves ($P < 0.01$).

TABLE 3

Static and dynamic lung volumes, maximum expiratory flow and transfer factor of the lung for pneumoconiotic and control miners.

Pneumoconiotics

Subject No.	V.C. (L)	F.R.C. (L)	R.V. (L)	R.V./T.L.C. %	T.L.C. (L)	$F.E.V_1$ (L)	$F.E.V_1$ (% pred)**	$\frac{FEV_1}{FVC}$ %	$MEF_{50\%}$ (L/sec)	$MMEF_{50-75\%}$ (L/sec)	T_L (ml/min/mm.Hg)
2	2.8	6.3	5.1	64.8	7.9	0.92	29	38	0.36	0.30	17.5
6	5.1	5.1	2.6	34.1	7.7	1.97	99	63	1.69	0.86	23.5
7	3.8	3.0	2.3	37.3	6.1	2.57	91	77	3.37	0.88	28.5
9	3.5	3.6	2.2	38.8	5.8	2.50	87	82	3.05	1.47	29
13	3.9	3.4	2.8	41.9	6.7	2.55	88	70	1.80	0.63	23.5
15	4.2	3.6	2.0	32.0	6.2	2.72	81	68	2.47	1.11	22
16	4.0	4.0	2.6	39.4	6.5	2.67	85	74	3.14	1.96	29.5
22	3.1	3.5	2.8	47.1	5.8	1.45	57	63			21
23	5.0	6.1	3.9	43.5	8.9	2.82	89	71	1.77	0.97	29.5
25	3.1	2.8	1.7	35.0	4.8	2.43	97	79	3.01	1.09	18.5
29	2.9	4.9	4.6	60.9	7.5	1.32	46	46	0.54	0.29	30.5
32	5.2	3.8	2.2	29.4	7.3	3.55	105	79	3.41	1.80	21
34	5.2	6.3	3.4	39.3	8.6	1.58	88	51	2.24	1.09	16
42	5.0	4.0	2.5	33.6	7.5	3.45	110	72	3.26	1.07	19
44	5.2	3.2	2.2	29.6	7.4	1.43	53	44	1.80	0.88	20.5
45	3.5	3.5	3.0	46.7	6.5	2.60	92	83	3.32	1.81	28.5
48	3.5	3.4	2.5	41.7	6.0	2.62	102	74	3.56	0.86	18.5
52	4.3	3.9	2.5	37.4	6.8	2.97	102	72	2.44	1.08	23
58	3.7	5.0	3.9	51.5	7.6	2.57	89	67	2.57	1.18	23
Mean	4.1	4.2	2.9	41.4	7.0	2.45	83	67.0	2.43	1.07	23.0
S.D.	0.84	1.11	0.91	9.6	1.03	0.70	21.7	13.2	0.95	0.46	4.6

TABLE 3 (contd.)

Controls

Subject No	V.C. (L)	F.R.C. (L)	R.V. (L)	R.V./T.L.C. %	T.L.C. (L)	F.E.V_1 (L)	F.E.V_1 (%pred)	$\frac{FEV_1}{FVC}$ %	$MEF_{50\%}$ (L/sec)	$MMEF_{50-75\%}$ (L/sec)	T_L (ml/min/mm.Hg)
1	3.5	3.2	2.7	43.1	6.1	2.03	77	73	1.71	0.84	34.5
3	4.7	3.7	2.2	32.0	6.9	3.07	95	73	–	–	34.5
4	4.1	4.6	2.9	41.6	7.0	2.80	94	74	2.40	1.09	32.5
5	4.5	3.9	1.6	37.0	7.1	2.78	96	75	2.83	1.24	22.5
8	4.5	3.3	2.4	34.9	7.0	3.10	115	77	3.47	1.53	33
10	4.9	4.2	2.4	33.2	7.3	3.27	114	71	–	–	28
11	5.0	4.9	2.8	36.2	7.9	3.05	97	65	2.22	1.05	17.5
12	3.4	3.5	2.2	39.0	5.6	1.95	75	73	–	–	29
14	5.4	6.7	4.0	42.6	9.4	3.67	102	66	2.68	1.37	29
17	4.8	3.5	3.4	41.4	8.4	2.77	85	67	1.59	0.86	28.5
18	4.1	2.9	2.0	32.6	6.0	2.62	80	70	2.47	0.68	28.5
19	3.5	3.4	3.0	46.7	6.5	1.73	62	54	1.25	0.66	19.5
20	4.4	2.4	1.9	30.7	6.3	3.43	132	83	4.73	2.40	32
21	4.9	4.0	3.5	41.5	8.3	3.02	100	66	1.46	0.55	24.5
24	3.2	4.5	3.3	50.2	6.5	2.20	81	59	1.02	0.54	25.5
26	5.6	3.9	2.5	30.9	8.1	3.30	118	72	2.72	1.10	25.5
27	5.0	4.5	3.0	37.5	7.9	2.68	95	58	1.76	1.11	27.5
28	4.5	4.0	2.3	34.1	6.9	2.85	106	65	1.72	1.07	20.5
30	4.0	4.1	2.9	41.8	6.9	2.07	80	56	0.68	0.33	24
31	3.7	3.0	2.3	37.8	6.0	2.75	105	74	1.81	1.25	27
33	3.6	3.4	2.8	43.7	6.4	2.40	95	68	–	–	27.5
35	3.8	2.6	2.1	35.9	5.9	2.63	104	78	–	–	31
36	4.0	7.2	6.1	60.1	10.1	2.42	92	66	1.06	0.49	30
37	3.8	4.4	2.9	43.7	6.7	2.90	98	82	3.18	1.66	23
38	–	–	–	–	–	2.70	93	77	4.69	1.61	–
39	4.3	4.4	1.8	29.5	6.1	2.70	104	73	–	–	22.5
40	3.4	3.9	2.7	44.5	6.2	1.88	74	59	0.92	0.46	14.5
41	4.7	5.2	3.2	40.2	7.9	2.73	85	59	1.41	0.55	28
43	3.5	3.3	2.8	45.0	6.3	2.60	85	76	5.77	3.09	39

TABLE 3 (contd.)

Subject No.	V.C. (L)	F.R.C. (L)	R.V. (L)	R.V./T.L.C. %	T.L.C. (L)	F.E.V.$_1$ (L)	F.E.V.$_1$ (%pred)	$\frac{FEV_1}{FVC}$ %	$MEF_{50\%}$ (L/sec)	$MMEF_{50-75\%}$ (L/sec)	T_L (ml/min/mm.Hg)
46	4.2	3.5	2.4	36.3	6.5	2.67	90	78	4.10	2.25	26
47	3.9	2.5	2.0	34.1	5.9	2.23	82	59	0.99	0.59	29
49	4.3	3.5	2.3	34.7	6.5	2.77	88	77	3.04	1.65	29.5
50	6.3	6.3	3.6	36.5	9.9	3.48	109	61	2.02	0.81	24
51	6.4	5.0	2.9	31.2	9.3	4.00	121	73	3.44	2.22	36
53	4.0	4.2	2.8	41.0	6.7	2.38	73	60	1.01	0.47	14.5
54	5.0	3.5	2.2	30.3	7.2	3.45	115	75	2.49	1.75	28.5
55	3.9	2.9	2.3	37.4	6.2	2.22	90	72	1.67	0.89	20
56	5.1	5.7	4.1	44.8	9.2	2.77	92	57	2.26	0.57	19.5
57	3.7	3.7	2.1	36.7	5.8	1.98	76	60	1.04	0.45	26.5
Mean	4.3	4.0	2.75	38.7	7.1	2.71	95	68.7	2.32	1.13	26.7
S.D.	0.77	1.09	0.79	6.2	1.21	0.52	15.1	7.8	1.24	0.66	5.7
P Values*	N.S.	N.S	N.S	N.S	N.S.	N.S	<0.05	N.S	N.S.	N.S	0.05

* Two sample t test ** from J.E. Cotes (1968)

TABLE 4

Occurrence of respiratory symptoms for pneumoconiotic and control groups of miners

Pneumoconiotics

Subject No.	Respiratory Symptoms * Cough	Phlegm	Wheeze	Weather	Dyspnoea	Chest illness	Average No. of resp. symptoms/ subject
2	x	x	x	x	x		
6	x	x	x	x	x	x	
7	x	x	x	x	x		
9	x	x	x	x	x		
13	x	x	x	x	x		
15	x	x	x	x	x	x	
16	x	x	x			x	
22			NA				
23	x	x	x	x	x	x	
25	x	x	x	x		x	
29	x	x	x		x		
32			x		x	x	
34	x	x	x	x			
42	x	x	x	x			
44					x		
45	x	x		x	x	x	
48	x	x	x	x	x		
52			x		x		
58	x	x	x	x	x		
% total	82	82	89	72	78	39	4.4

Controls

Subject No.	Cough	Phlegm	Wheeze	Weather	Dyspnoea	Chest illness	Average No. of resp. symptoms/ subject
1			x				
3			NA				
4		x					
5				x			
8							
10			NA				
11	x	x	x		x		
12			NA				
14	x	x	x	x			
17				x	x	x	
18							
19			x				
20			x				
21					x		
24	x	x	x	x	x		
26							
27	x	x			x		
28		x	x	x			
30	x	x	x	x	x	x	
31				x			
33			NA				

TABLE 4 (page 2)

Respiratory Symptoms *

Subject No.	Cough	Phlegm	Wheeze	Weather	Dyspnoea	Chest illness	Average No. of resp. symptoms/ subject
35			NA				
36	x	x					
37	x	x		x	x	x	
38	x	x	x	x	x	x	
39			NA				
40	x	x	x		x		
41	x	x	x	x			
43							
46	x	x					
47	x	x	x	x	x	x	
49			x				
50							
51	x		x	x			
53	x	x					
54	x	x	x	x	x		
55							
56							
57	x		x				
% total	48	48	51	39	33	12	2.3
P values**	<0.05	<0.05	<0.05	NS	<0.01	NS	

*For definition see page 37 of Discussion. **Fourfold test of significance (chi square test). N.A. - not available.

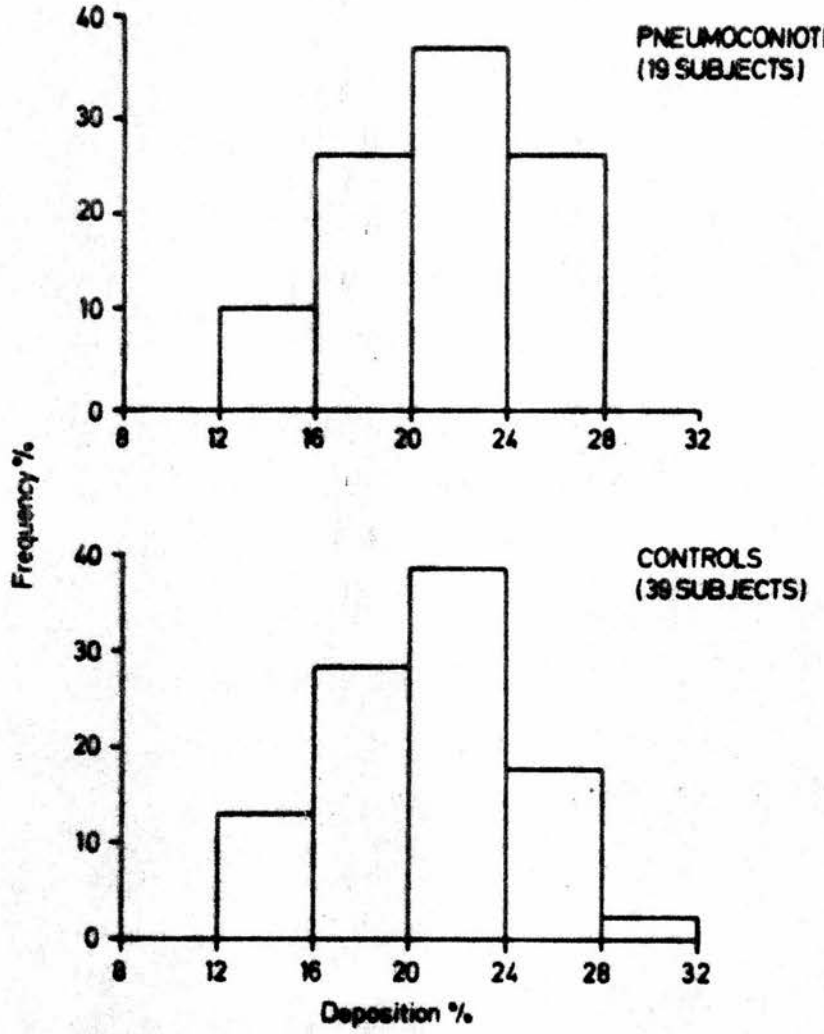

Fig.15 Histogram of total deposition for two groups of coalworkers

5.2 Comparison of the two populations

The two groups of pneumoconiotic and non-pneumoconiotic or control subjects were selected to be matched for age and as far as possible for occupational history. Comparison of the groups on the basis of age, height, weight, smoking habits and years worked underground and at the coal face are shown in Table 2. Results of lung function tests, which were performed on each subject are compared in Table 3.and the results of a questionnaire on respiratory symptoms are shown for the two groups in Table 4.

There were no significant differences between the groups on the basis of age, height, weight, smoking habits or years of work underground, so that these groups may be considered to be matched groups drawn from the same population.

Aerosol deposition has been plotted in the form of a frequency distribution for the two groups of pneumoconiotics and controls in Fig. 15 and individual values are shown in Table 2. The average deposition was 20.9% for the control and 21.3% for the pneumoconiotics. At tidal volumes of 1.0 and 2.2 litres the average deposition was 19.8 and 23.1% respectively for the control group, and 19.4 and 23.1% for the pneumoconiotic group. This represents a slightly greater rate of increase of deposition with tidal volume for the pneumoconiotics but the differences in percentage deposition between the two groups are insignificant (two sample t test). Therefore at tidal volumes within the normal working range there is no more than a difference of 1% fractional deposition between a group of coalworkers with simple pneumoconiosis and a matched group without pneumoconiosis.

The variation in the shape of the expired aerosol concentration curve (Shape Factor) is shown in Table 2. It can be seen that there are nearly twice as many subjects with convex curves compared with concave in the control group but approximately the same number of each in the pneumoconiotic group. There is, therefore, a tendency for there to be a greater number of subjects with intermediate and concave curves among this group of pneumoconiotics, although the differences were not significant (chi square test).

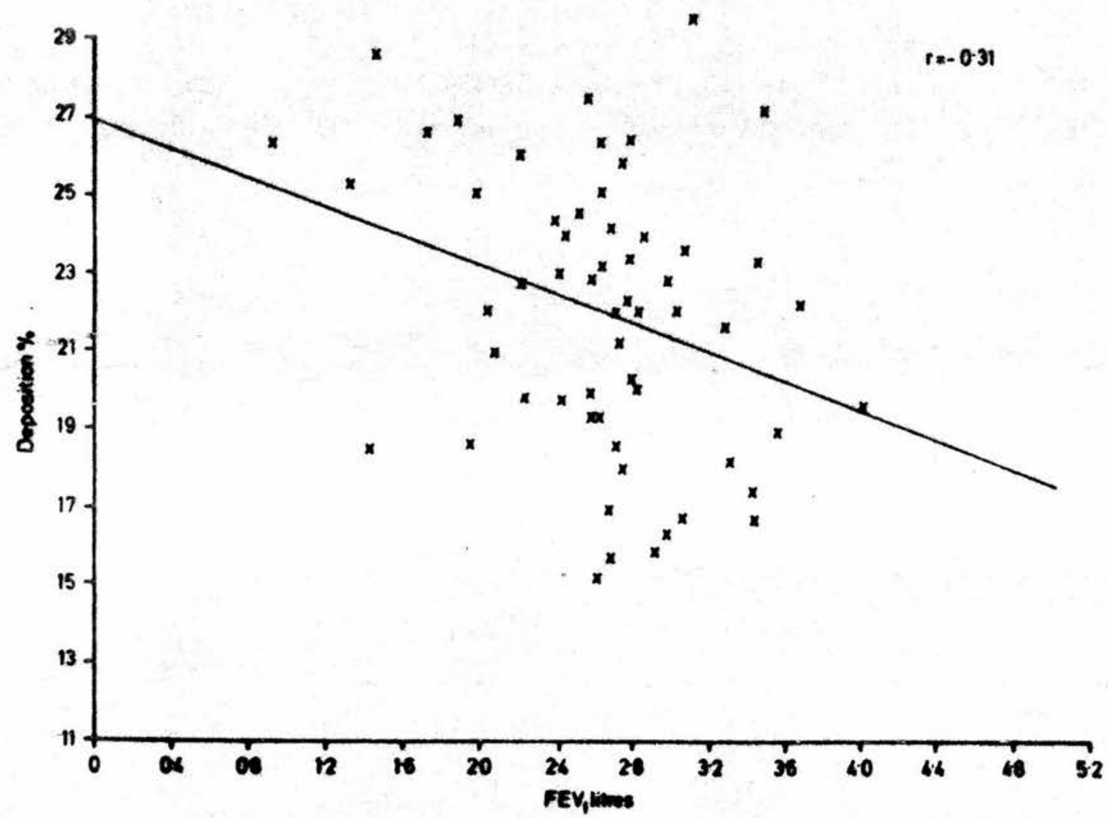

Fig. 16 **Relationship between total deposition and FEV_1 for 58 coalworkers**

The regression line has been fitted using the method of least squares.

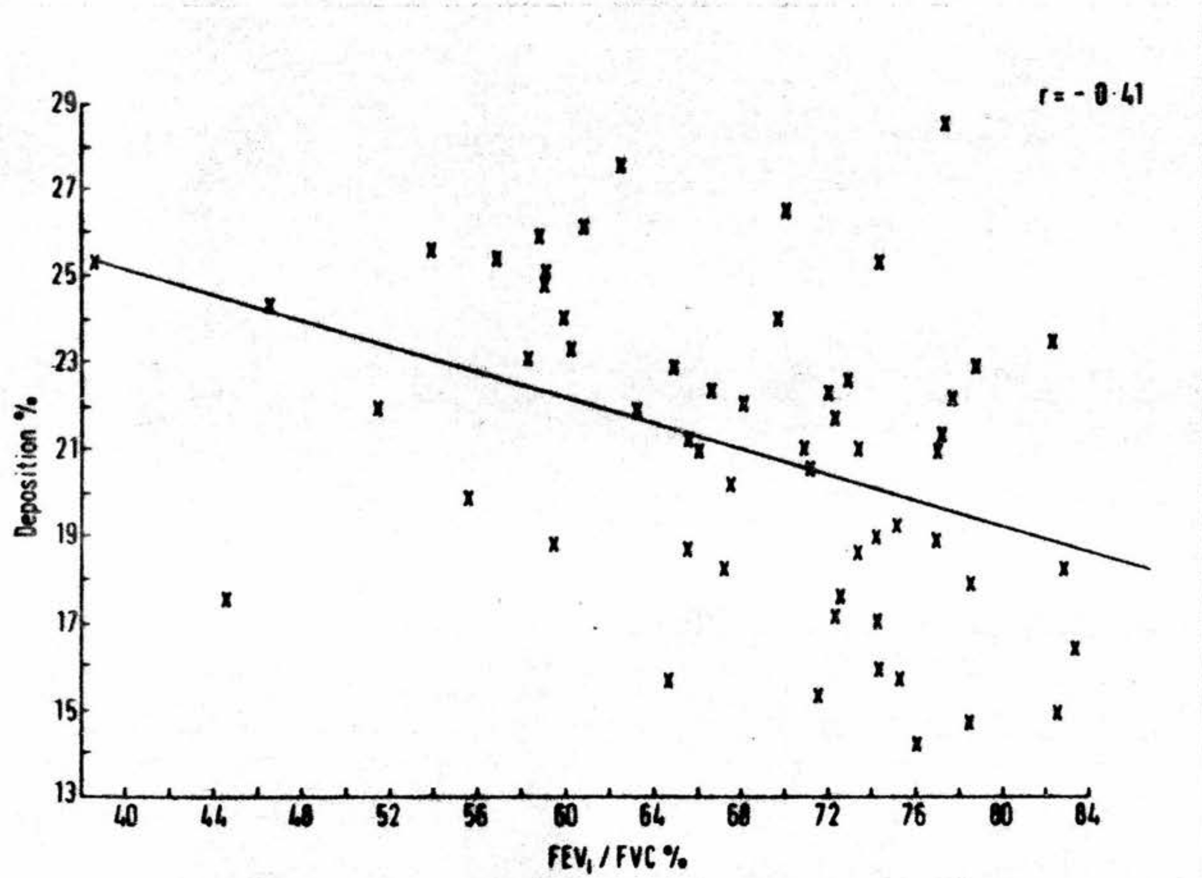

Fig. 17 Relationship between total deposition and FEV$_1$% for 58 coalworkers

The regression line has been fitted using the method of least squares.

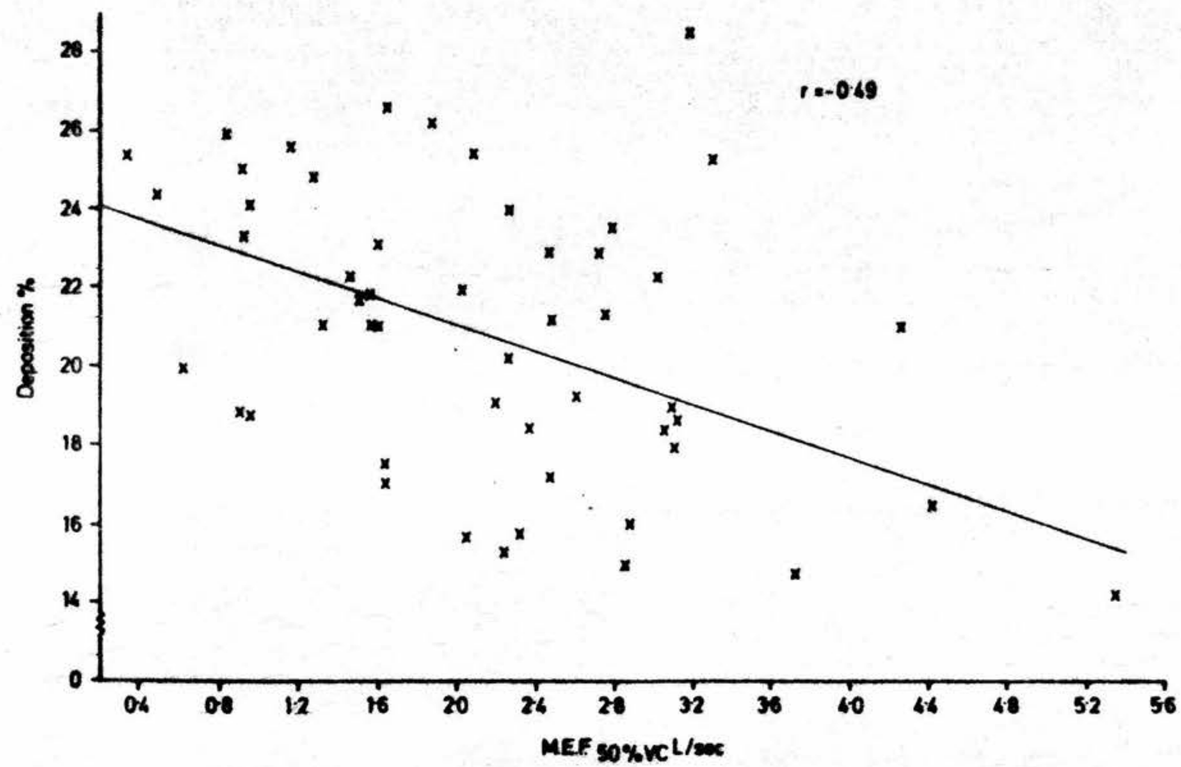

Fig.18 **Relationship between total deposition and MEF**$_{50\%}$ **for** 51 **coalworkers**

The regression line has been fitted using the method of least squares.

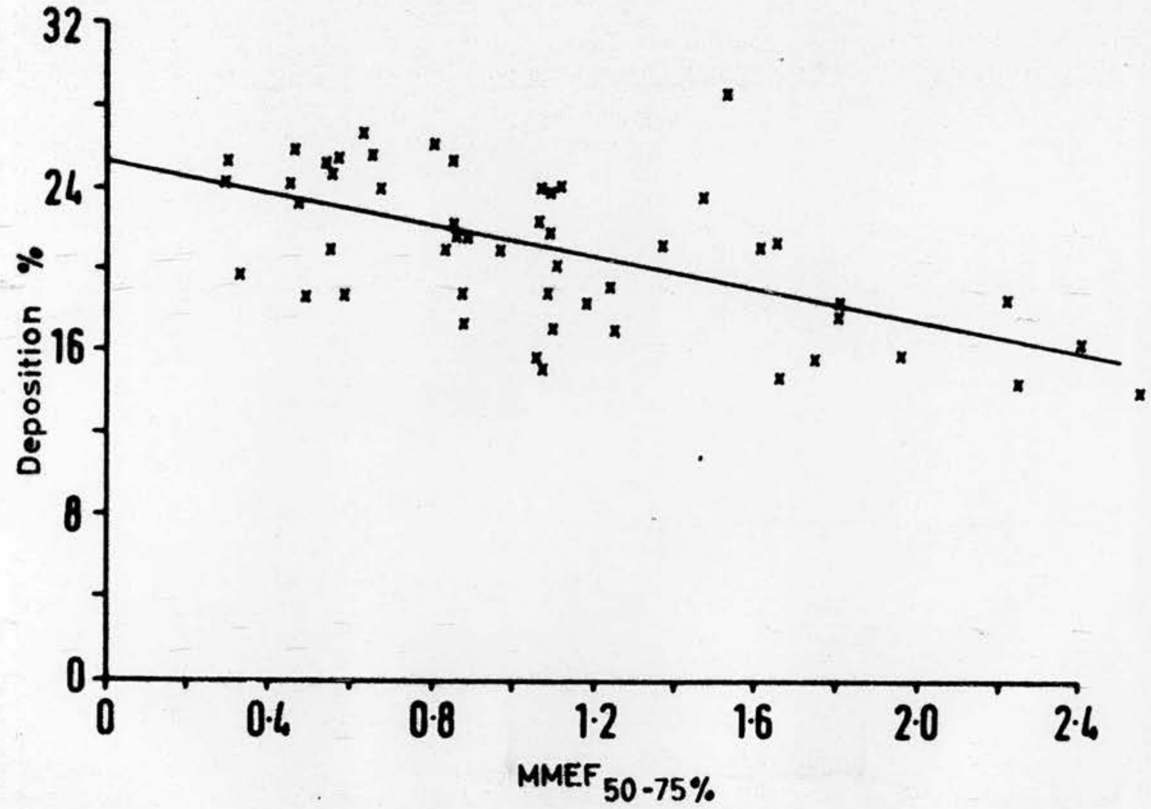

Fig.19 Relationship between total deposition and $MMEF_{50-75\%}$ for 51 coalworkers

The regression line has been fitted using the method of least squares.

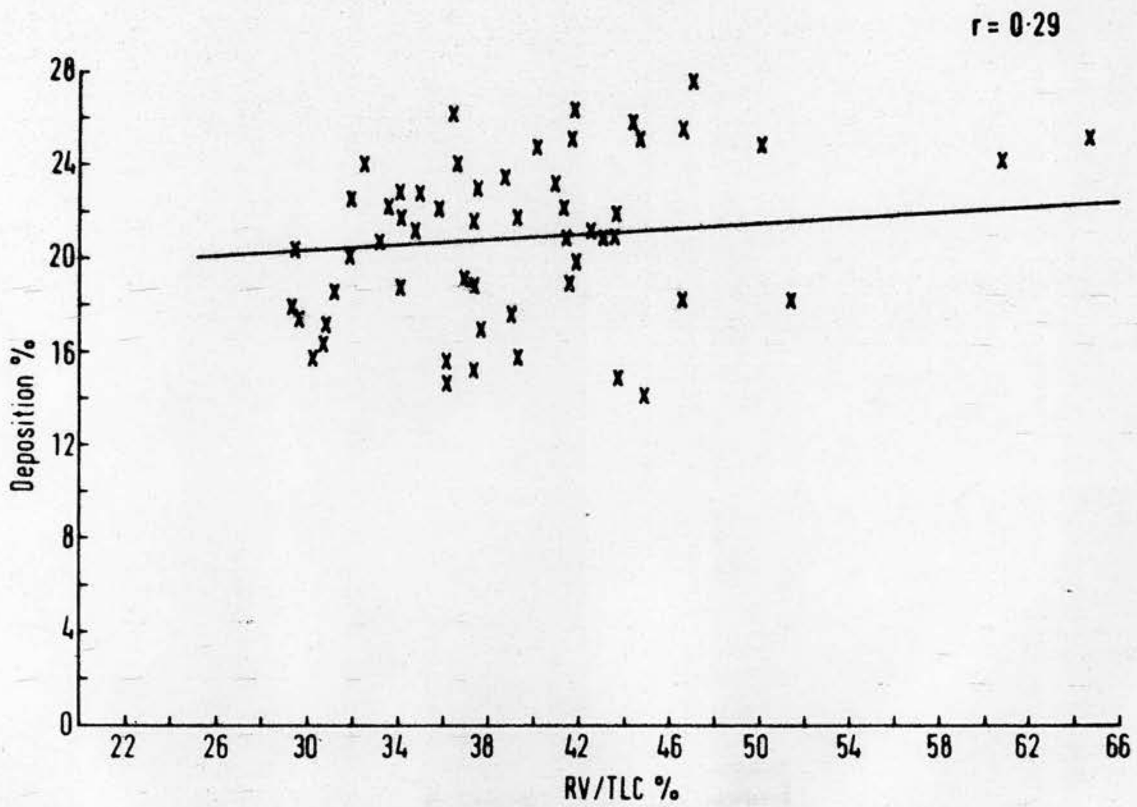

Fig. 20 Relationship between total deposition and RV/TLC% for 55 coalworkers

The regression line has been fitted using the method of least squares.

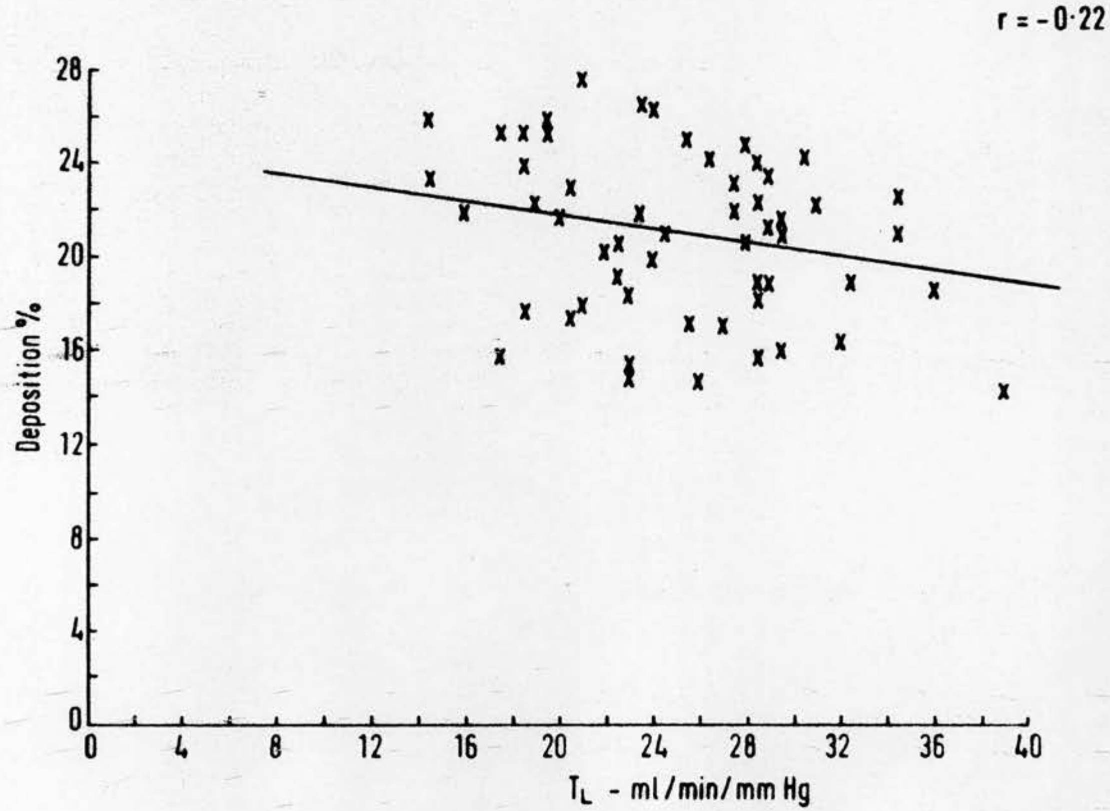

Fig. 21 Relationship between total deposition and transfer factor for 55 coalworkers

The regression line has been fitted using the method of least squares.

TABLE 5

Tests of significance of correlation coefficients for each lung function variable in relation to percentage aerosol deposition (D)

Variable (x)	Correlation coefficient r	P*	Regression Equation
FEV_1	-0.31	< 0.02	D = −1.86x + 25.87
FEV_1/FVC %	-0.41	< 0.001	D = −0.15x + 31.11
$MEF_{50\%}$	-0.49	< 0.001	D = −1.69x + 24.44
$MEF_{50-75\%}$	-0.60	< 0.001	D = −3.72x + 25.07
RV/TLC %	0.29	< 0.05	D = 1.57x − 41.45
T_L	-0.22	N.S.	D = −0.14x + 24.66

* Probability that this value of r could occur by chance.

TABLE 6

Lung function, respiratory symptoms, smoking habits and aerosol deposition for 18 miners with convex shape factor.

Subject	Deposition %	FEV_1 % pred.	MMEF 50-75% L/sec	RV/TLC %	T_L ml/min/ mm Hg	Smokers*	Respiratory Symptoms † C	P	Wh	W	B	I
1	21.0	77	0.84	43.1	34.5	x			+			
3	22.6	95	-	32.0	34.5	-			N.A.			
4	19.0	93	1.09	41.6	32.5	+		+				
5	19.2	96	1.24	37.0	32.5	+					+	
7	18.9	91	0.88	37.3	28.5	x	+	+	+	+	+	
12	17.6	75	-	39.0	18.5	x			N.A.			
16	15.9	84	1.96	39.4	29.5	+	+	+	+			+
20	16.4	132	2.40	30.7	32	-			+			
31	17.0	104	1.25	37.8	27	-				+		
32	17.9	105	1.80	29.4	21	+			+		+	+
37	14.9	98	1.66	43.7	23	+	+	+	+		+	+
38	21.0	92	1.61	-	-	+	+	+	+	+	+	+
39	17.6	104	-	29.5	22.5	+			N.A.			
43	14.2	85	3.09	45.0	39	-						
46	14.7	90	2.25	36.3	26	-						
51	18.6	121	2.22	31.2	36	+	+	+				
52	15.3	102	1.08	37.4	23	+	+		+	+		
54	15.7	115	1.75	30.3	28.5	-	+	+	+	+	+	
Mean	17.6	97	1.68	36.5	28.2	50%			2.2			
S.D.	2.4	14.6	0.64	5.2	5.9	-			2.1			

* + = Smoker X - Ex-smoker - = Non-Smoker † See Table 4 N.A. = not available.

TABLE 7

Lung function, respiratory symptoms, smoking habits and aerosol deposition for 25 miners with intermediate shape factors.

Subject	Deposition	FEV_1	MEF 50-75%	RV/TLC	T_L ml/min/ mm Hg	Smoking *	Respiratory Symptoms ⨍					
	%	% pred.	L/sec	%		%	C	P	Wh	W	B	I
6	21.8	98	0.86	34.1	23.5	+	+	+	+	+	+	+
9	23.5	87	1.47	38.8	29	+	+	+	+	+	+	
10	20.6	114	-	33.2	28	+						
11	15.7	97	1.05	36.2	17.5	x	+	+	+		+	
14	21.2	101	1.37	41.6	29	+	+	+	+	+		
15	20.2	81	1.11	32.0	22	x	+	+	+	+	+	+
18	24.0	79	0.68	32.6	28.5	+						
21	21.0	100	0.55	41.5	24.5	+					+	
23	21.0	89	0.97	43.5	29.5	x	+	+	+	+	+	+
25	22.9	97	1.09	35.0	18.5	+	+	+	+	+		+
26	17.2	118	1.10	30.7	25.5	+						
28	22.9	106	1.07	34.1	20.5	+		+	+	+		
30	19.9	80	0.33	41.8	34	+	+	+	+	+	+	+
33	22.0	95	-	43.7	27.5	+			N.A.			
34	21.9	87	1.09	39.3	16	+	+	+	+	+		
35	22.2	104	-	35.9	31	+			N.A			
36	18.7	92	0.49	60.1	30	+	+	+				
42	22.3	110	1.07	33.6	19	+	+	+	+	+		
44	17.5	53	0.88	29.6	20.5	+						
45	18.3	92	1.81	46.7	28.5	x	+	+		+	+	+
47	18.8	82	0.57	34.1	29	+	+	+	+	+	+	+
49	21.3	81	1.65	36.8	29.5	+			+			
55	21.7	89	0.89	37.4	20	+						
57	24.1	76	0.45	36.7	26.5	+	+		+			
58	18.3	88	1.18	51.5	23	+	+	+	+	+	+	
Mean	20.7	92	0.98	38.5	24.8	84			3.3			
S.D.	1.8	14	0.38	6.9	4.5				2.3			

* See Table 6 ⨍ See Table 4 N.A. Not available

TABLE 8

Lung function, respiratory symptoms, smoking habits and aerosol deposition for 13 miners with concave shape factor.

Subject	Deposition	FEV_1	MMEF 50–75%	RV/TLC	T_L ml/min/mm Hg	Smokers *	Respiratory ⨍ Symptoms					
	%	% pred.	L/sec	%			C	P	Wh	W	B	I
2	25.3	29	0.30	64.8	17.5	+	+	+	+	+	+	
13	26.5	88	0.63	41.9	23.5	+	+	+	+	+	+	
19	25.6	62	0.66	46.7	19.5	+			+			
22	27.6	57	-	47.1	21	+			N.A.			
24	25.0	81	0.54	50.2	25.5	+	+	+	+	+	+	
27	23.1	94	1.11	37.5	27.5	–	+	+				+
29	24.3	46	0.29	60.9	30.5	–	+	+	+		+	
40	25.9	74	0.46	44.5	14.5	+	+	+	+		+	
41	24.8	84	0.55	40.2	28	+	+	+	+	+		
48	25.3	101	0.86	41.7	18.5	x	+	+	+	+	+	
50	26.2	109	0.81	36.5	24	+						
53	23.3	73	0.47	41.0	14.5	+	+	+				
56	25.4	92	0.57	44.8	19.5	+						
Mean	25.3	76	0.60	46.0	21.9	77%			3.2			
S.D.	1.1	23.0	0.24	8.8	5.4	–			1.9			

* See Table 6 ⨍ See Table 4 N.A. Not available

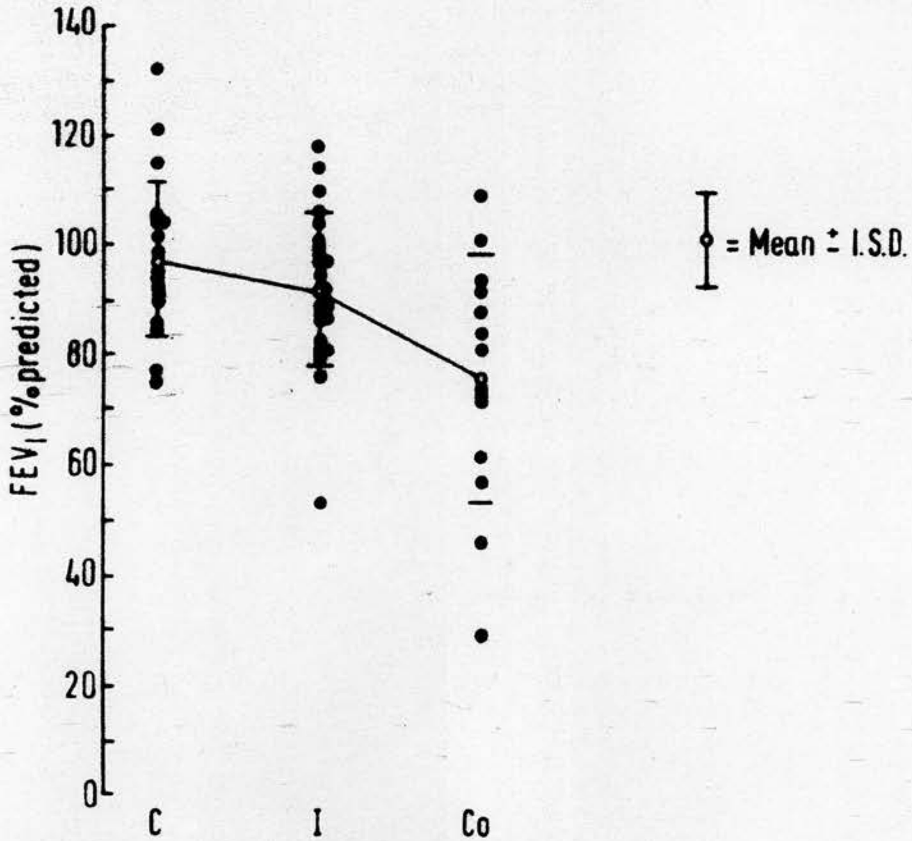

Fig.22 Relationship between shape factor and FEV_1.
(C = convex: I = Intermediate: Co = concave)

ng page 26

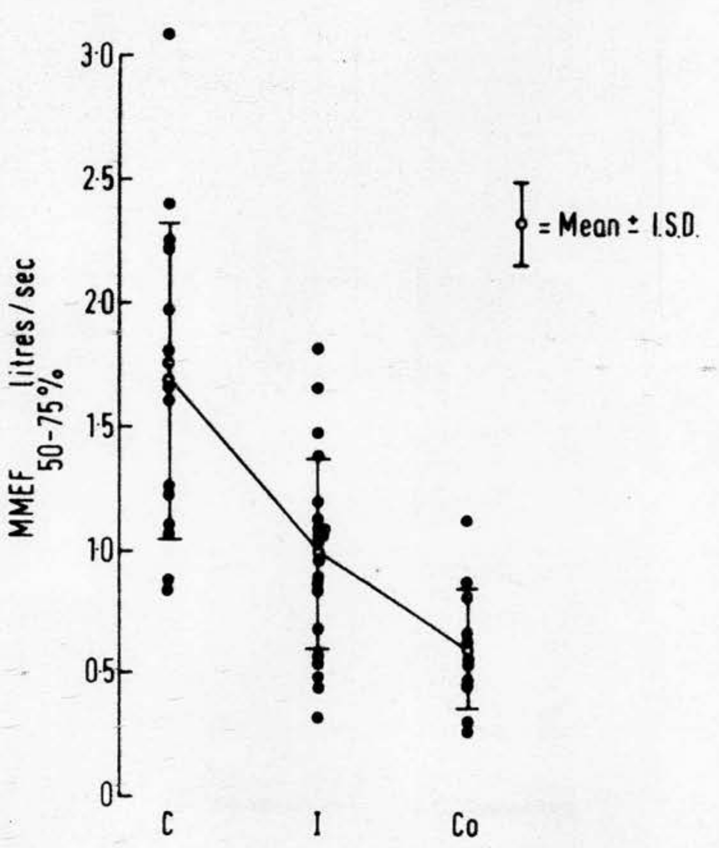

Fig. 23 Relationship between shape factor and $MMEF_{50-75\%}$

(C = convex: I = Intermediate: Co = concave)

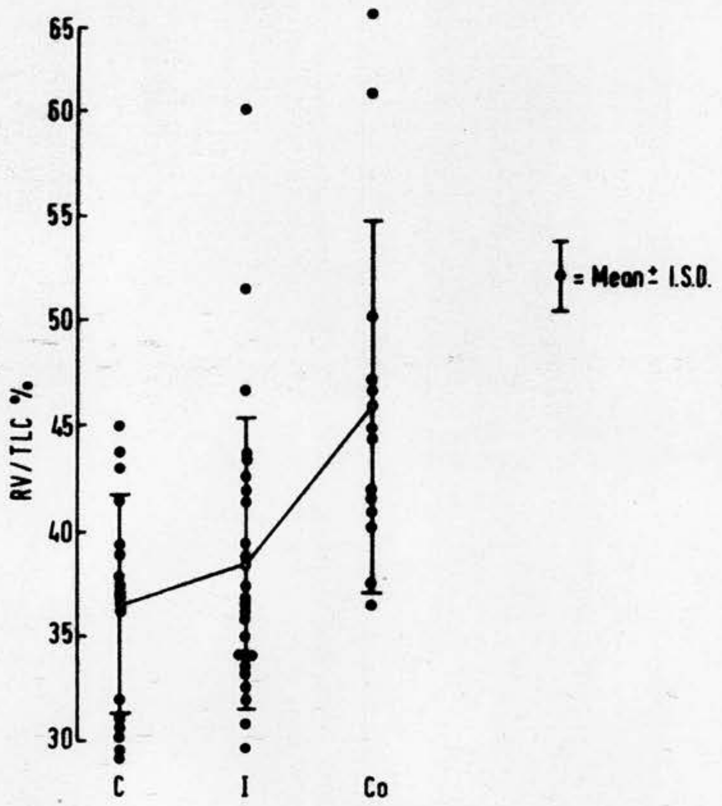

Fig.24 Relationship between shape factor and RV/TLC%
(C = convex: I = Intermediate: Co = concave)

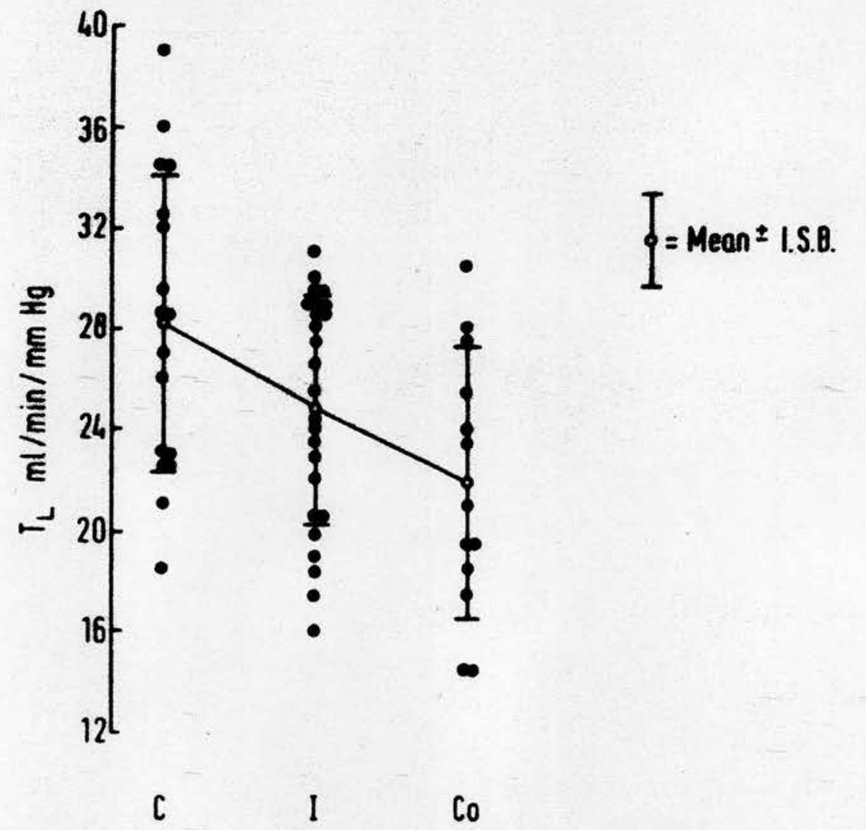

Fig. 25 Relationship between shape factor and transfer factor.
(C = convex: I = intermediate: Co = concave)

TABLE 9

Statistical significance of differences in deposition and lung function variables between groups with convex (C), intermediate (I) and concave (Co) shape factors (Sheffé method for multiple comparisons).

Level of Significance	Deposition	FEV_1	$MMEF_{50-75\%}$	RV/TLC	T_L
< 0.05	N.S.*	C & Co+	N.S.	I & Co	C & Co
< 0.01	C & I	N.S.	N.S.	C & Co	N.S.
< 0.001	I & Co	N.S.	C & I I & Co	N.S.	N.S.

* N.S. = not significant at stated level

\+ Difference between groups is significant at stated level.

TABLE 10

The relationship between respiratory symptoms and aerosol deposition and associated pulmonary function.

No. of Symptoms	No. of Subjects	Deposition (%)	Shape C	Factor* I	CO	FEV_1 (L)	$MMEF_{50-75\%}$ (L/sec)	RV/TLC (%)
0	6	21.5	1	3	2	2.82	1.36	37.3
1-2	13	20.2	7	4	2	2.58	1.09	39.5
3-4	13	21.0	3	6	4	2.78	1.06	39.7
5-6	17	21.0	4	9	4	2.52	1.04	41.7
P		NS				NS	NS	NS

* C = Convex; I = Intermediate; Co = Concave

NS = Not significant

TABLE 11

The effects of smoking on aerosol deposition and associated pulmonary function.

Group	No. of Subjects	Deposition	FEV_1	$MMEF_{50-75\%}$	RV/TLC	T_L	Shape	Factor*	
		(%)	(L)	(/sec)	(%)	ml/min/ mm/Hg)	C	I (%)	Co
Non-Smokers	8	18.5	2.75	1.73	38.8	30.8	75	0	25
Ex-Smokers	7	19.9	2.54	** 0.95	39.0	24.1	43	43	14
Smokers	42	** 21.6	2.62	$\not-$ 0.98	39.9	$\neq$ 24.3	22	54	24

* C = Convex; I = Intermediate; Co = Concave. Differences from values of non-smokers are significant at the following levels. ** = $P < 0.05$; $\not-$ = $P < 0.01$; $\neq$ = $P < 0.001$

5.3 Aerosol deposition and other indices : lung function, respiratory symptoms, smoking habits.

(a) Lung Function

Lung function studies were carried out on each subject and the results of these are shown for the two groups in Table 4. It can be seen that, although there are only small differences between the groups, which are insignificant for the size of this population, there is on average a significantly lower than normal FEV_1 (% predicted) and reduced transfer factor for the pneumoconiotic group. ($P < 0.05$)

The further measurements of dynamic lung function made 6 - 8 months later on 51 out of 58 of the original subjects are also shown in Table 4. There was virtually no difference in FEV_1 between the groups compared with the earlier measurement although there were some individual differences nor was there any significant difference in the maximum expiratory flow at 50% of Vital capacity (MEF 50%) nor between 50% and 75% of the vital capacity (MMEF 50-75%) for the two groups.

The relationship between aerosol deposition and lung function was investigated and the results are illustrated in Figs. 16-21, which show the relationship between deposition and FEV_1, $FEV_1\%$, $MEF_{50\%}$, $MMEF_{50-75\%}$, RV/TLC % and T_L (transfer factor). The correlation coefficients for each variable and its statistical significance are shown in Table 5, which also includes the regression equation relating each variable to deposition.

The relationship between shape factor and lung function is shown in Tables 6 - 8 and is illustrated in graphical form in Figs. 22-25. Increasing abnormality was apparent as shape factor tended from convex to concave for [redacted] FEV_1, $MMEF_{50-75\%}$, RV/TLC % and T_L with significant differences between subjects with convex and concave types of curve for all variables, although only $MMEF_{50-75\%}$ showed significant differences between subjects with each of the three groups ($P < 0.001$). (Table 9).

(b) Respiratory Symptoms

The relationship between aerosol deposition and respiratory symptoms is illustrated in Table 10, which also shows that there was no significant correlation between symptoms and lung function in the population. There was no correlation between deposition and respiratory symptoms nor did the shape factor vary significantly with increasing number of symptoms.

(c) Smoking habits

Although a significant relationship between aerosol deposition and smoking habits was found and is shown in Table 11, there were relatively few non-smokers and ex-smokers. The increased deposition associated with smoking is largely accounted for by changes in lung function, since there were significant correlations between smoking and $MMEF_{50-75\%}$ ($P < 0.01$) and transfer factor ($P < 0.001$). There was also a smaller proportion of smokers with convex shape factor (22%) compared with non-smokers (75%).

CHAPTER 6

DISCUSSION

6.1 Comparability of the two groups of miners

The two groups of subjects selected for this study were drawn from five Scottish collieries and consisted predominantly of underground workers. Official records of occupational history for each subject were available from 1947 onwards and any previous history of underground work was given by the subject himself at the time of the study. Some men in the sample had worked in several collieries under varying conditions of dust exposure. Since records were unavailable, it has been assumed that the average dust exposure for the groups of pneumoconiotic and control coalworkers was similar. The mean number of years worked underground and at the coalface was about the same for the two groups (Table 2) as was their average age.

Anthropomorphically the groups were also comparable. The pneumoconiotics were on average slightly taller and heavier but the differences were statistically insignificant. On the basis of current smoking habits there was an equal proportion of smokers within each group and no significant difference in the proportions of ex-smokers (Table 2).

Tests carried out at the time of the study showed that indices of lung function were slightly abnormal on average, in the pneumoconiotic group although only FEV_1 as a percentage of predicted normal and transfer factor showed any statistically significant differences between the groups (Table 3).

The results of a questionnaire on respiratory symptoms (Table 4) demonstrated a considerable difference in the number of reported symptoms for the two groups. On average the pneumoconiotics reported nearly twice as many symptoms as the controls with significant differences ($P < 0.05$) being found for cough, phlegm, wheeze and dyspnoea. Only two out of 19 pneumoconiotics did not complain of persistent cough and phlegm and none of this group was completely symptom-free. It is a matter of conjecture as to whether or not the pneumoconiotic miners reported more symptoms because of an awareness of their medical condition. The disassociation of this study with the miner's own personal welfare was stressed at the time of the initial interview, so that any differences are likely to be related to true symptom difference, rather than to the 'iatrogenic effect', noted by Ashford et al (1970). That this difference is at least partly a real phenomenon was observed by Rae et al (1971) who found a highly significant difference in the prevalence of bronchitis symptoms in faceworkers with pneumoconiosis compared to those without pneumoconiosis.

6.2 The effect of pneumoconiosis on aerosol deposition and shape factor

The main aim of this study was to examine the individual variation of total respiratory deposition of particles in the lungs of coalworkers with and without simple pneumoconiosis. The principal finding has been that there is no significant difference in the total amount of aerosol deposited in the lungs of coalworkers in these two groups. The individual deposition values (Table 2) and their frequency distribution (Fig.15) show that the mean values and their ranges were similar for the pneumoconiotics and the controls. The difference between the mean deposition at a tidal volume of 1.6 litres was insignificant and, although the rate of increase of deposition with tidal volume was slightly greater for the pneumoconiotics, the difference was again insignificant.

It is clear therefore that coalworkers simple pneumoconiosis (categories 1 and 2) causes insufficient derangement of the normal lung architecture to give rise to real differences in total deposition.

It can, of course, be argued that this sample was not representative of coalminers as a group and that the pneumoconiotics in the sample did not present sufficient pathological abnormality for any significant changes to occur in the behaviour of inhaled airborne particles.

There is a low incidence of coalworkers pneumoconiosis in the coalfields of the Scottish area (Hicks et al 1961). The subjects with pneumoconiosis in this study were drawn from the five most local collieries and consisted of about half of all working miners with category 2 pneumoconiosis in these collieries. For this reason the total numbers available for study were limited. Half were unable to attend, owing to illness or recent retiral. Because of the low dust levels in the area most of the men studied were near the end of their working lives and their age range was relatively narrow, 48-64 years.

However, although they may be a selected group by age, they were matched by a control group of similar age.

Only coalworkers with X-ray changes within categories 1 and 2 were included. It was the aim of the study to examine the possible difference in aerosol deposition in miners with early signs of the disease before it had progressed to the stage, in which gross abnormalities and deformation of lung tissue could have been present. In other words the pathological changes due to coalworkers' pneumoconiosis in this group should have been limited to the region of the second or third order respiratory bronchioles (Heppleston, (1947), (1953)).

A question, which cannot be answered entirely satisfactorily, is whether or not the two groups had been subjected to similar exposures of coal dust during their working lives. It was only possible to match the groups for the numbers of years spent working underground or at the coalface. It had to be assumed that, on average, each group had been exposed to equal dust levels. The majority of miners in the study had worked in several collieries over a span of 30 to 50 years, many of them before dust levels were monitored, so that it is unrealistic to attempt any strict comparison.

Although it has been shown that aerosol deposition is not affected substantially by the presence of coalworkers' pneumoconiosis, this may not reflect the pattern of deposition before the miners contracted the disease. It could be postulated that the pneumoconiotic group had a deposition rate higher than the control group initially and that, subsequently, the presence of the disease had reduced the deposition rate. If this were true, the rate of progression of pneumoconiosis, assuming constant exposure to dust, would probably be reduced. It is now known that progression to a higher category is faster for miners, who already have evidence of pneumoconiosis (Jacobsen et al 1971). Therefore, deposition is unlikely to have been higher initially in the pneumoconiotics. It could, on the other hand, have been lower than the controls initially and have increased as the disease progressed. Again this explanation is unlikely, since it is hard to believe that the mean deposition and the range of values within the two groups would be so similar.

It cannot be assumed that the deposition in the control group of miners would be similar to that in a non-mining group. Continued exposure to coal dust may have altered the deposition pattern in both groups to the same extent. However, pneumoconiotics as a group do not have increased deposition and, since several control miners had high deposition, increased deposition does not necessarily lead to pneumoconiosis.

The study was limited to the investigation of the deposition of 1μ diameter particles in the lungs of coalworkers. Coalworkers' pneumoconiosis is not caused only by the accumulation of dust particles one micron in diameter, although analysis of lung dust deposits indicates that most of the dust is less than 2μ diameter (Cartwright and Nagelschmidt, 1961).

One micron diameter particles were used for this reason and also because they are believed to be near to the maximum for alveolar deposition (Davies, 1952). The La Mer-Sinclair aerosol generator produces a relatively homogenous aerosol at this size and the diameter of such particles is easily measured by the "Owl".

It does not necessarily follow that differences in aerosol deposition for one micron particles within this group of subjects would be similar if larger or smaller particles were used. However, studies on normal subjects have shown that individuals who have high deposition for one particle size, invariably exhibit high deposition for other particle sizes (Altshuler et al 1957). Similarly, the breathing frequency of the subjects was restricted to 15 breaths per minute. It does not follow that deposition at other respiratory rates would be in the same relationship, although previous work would suggest that this is the case (Altshuler et al 1957).

The aerosol particles used in the experiment were spherical oil droplets with a density of 0.92 g. cm^{-3}. Coal dust particles which deposit in the lungs are unevenly shaped, often with one axis longer than the other and with a density greater than unity (1.2 - 1.4 g. cm^{-3}). However, the differences in physical behaviour that exist between spherical and irregular particles are not important in the present context. The behaviour of inhaled particles and the probability that a single particle will be able to penetrate to the alveolus depends on its aerodynamic properties. Modern dust control measures in the industry are based on the recognition of this fact. Dust sampling techniques are related to the falling velocities of the particles and not to their apparent microscopic size or shape. The physical basis of this concept is explained in Chapter 1. It follows that it is perfectly valid to use an artificial aerosol of spherical droplets and to make use of the findings in breathing experiments for the interpretation of the behaviour of coal dust in the lungs.

The pattern of aerosol deposition, represented by the shape of the aerosol recovery curve (Shape factor), differed for the two groups. Only 4 out of 19 (21%) pneumoconiotics had curves of the convex type compared with 14 out of 37 (38%) in the control group.

The interpretation of this finding is difficult at present but has interesting implications. It will be recognised that the results have been expressed in terms of the total deposition of particles in the lungs. There is no direct method at present of estimating the actual pattern of deposition within the lung spaces. It is possible, for example, that two individuals might have an identical total deposition, but that one subject might deposit a greater percentage of the inhaled material within the alveolar spaces. Such an individual, while apparently retaining the same amount of dust, would be at a greater risk of developing pneumoconiosis because the alveolar dust load would, of course, be greater.

There have been attempts to estimate the regional deposition of particles in the lung by observations of the aerosol recovery in the expired air. This work, by Brown et al (1950) and Altshuler et al (1957) is described in detail in Chapter 2. The finding that the pneumoconiotics, as a group, had a greater proportion of abnormal curves than the control group suggests that further work into this aspect would be worthwhile.

6.3 <u>Individual variability</u>

The deposition values varied from 14% to 28% (See Fig.15). It is important to consider whether or not this range represented a true difference between individuals or whether it was due to the experimental technique. There may well have been small changes in particle size during the course of each experiment, but these alone are unlikely to have led to the observed wide individual variations in total respiratory deposition since it was shown that deposition was well correlated with lung function and this suggests that the individual differences are real. The main concern of this work is a comparative one, so that even if the deposition values were an under- or over-estimate of the true figures the comparison of the groups is still valid.

The reliability or repeatability of the measurements of deposition could have been tested by a subsequent re-examination of the two groups. This was impracticable because the subjects were all working miners and it did not prove possible to recall them for further tests.

The deposition rates reported have ranged from about 14% -- 28%, a twofold ratio between the highest and lowest values. Brown et al (1950); Altshuler et al (1957); Dautrebande and Walkenhorst (1961); Dennis (1961); Beeckmans (1965) and several other workers in theoretical and experimental studies have reported deposition values for 1μ diameter particles of between 26% and 53% in normal subjects. The wide range of these results is probably due to the different techniques used. The results presented here fall at the lower end of this range but are based on over 240 experiments on 58 subjects. The method involved a continuous monitoring of a monodisperse aerosol by an optical means and it should be noted that the values obtained were close to those of Altshuler et al (1957) who used a similar method of measurement.

Previous published work on total aerosol deposition has been confined to normal healthy subjects who had no specific evidence of lung disease or of abnormal lung function. Results of such studies, in which values were reported for individual subjects (Landahl et al (1951); Altshuler et al (1957), and Muir (1966) have shown that there can be wide variations in the amount of inhaled aerosol deposited for any particular size and over a wide range of particle diameters.

However studies which employed an optical method of measurement have shown, in normal subjects, (Altshuler et al (1959)) that there are significant individual variations in the distribution of aerosol in the exhaled air during steady state breathing. This has been demonstrated more clearly in patients with asthma and bronchitis (Muir, 1970) for single breaths of aerosol and a more extensive analysis of single breaths has recently been reported for a group of coalworkers by Cotes et al (1971). These authors graded the expired aerosol curves visually and found that they were correlated with FEV_1.

The distribution of aerosol in the exhaled air of the miners in the present study was also examined and the results are discussed in detail in section, 6.4.

6.4 The relationship between aerosol deposition and other factors.

(i) Lung Function

The association between aerosol deposition and lung function, which is illustrated in Figs.16-21, and between shape factor and lung function, illustrated in Tables 6-8 and Figs. 22-25, accounted for most of the individual differences in deposition for the subjects in this study. The closest correlation ($P < 0.001$) was found to be between deposition and measurements of lung function which primarily reflect airways obstruction: $FEV_1\%$, $MEF_{50\%}$ and $MMEF_{50-75\%}$. Althouth there were significant differences of FEV_1, $MMEF_{50-75\%}$, RV/TLC% and T_L for subjects with concave and convex shape factors there was considerable overlap and only $MMEF_{50-75\%}$ showed significant differences between all three shape factors.

Muir (1970) had originally observed marked differences in the shape of the expired aerosol concentration curve for single breaths of aerosol in patients with overt signs of airway obstruction (Mean FEV_1 = 27% predicted) compared with normal subjects. Cotes et al (1971) later demonstrated in selected coalworkers that a significant correlation existed between FEV_1 and a visual grading of the single breath expired concentration curve. However, this thesis is the first study of a normal working population of coal-workers in which a comprehensive series of lung function measurements has been made and an association with aerosol deposition and shape factor found during normal breathing.

The close correlation between aerosol deposition and $MMEF_{50-75\%}$ would suggest that increased deposition in the lungs of these coal-workers is due to obstruction in the small, peripheral airways. It is currently believed that measurement of airflow at or near to the end of a maximum forced expiration primarily reflects the resistance to flow in small airways, probably those less than 2mm diameter Fry (1958); Hyatt et al (1958); Fry and Hyatt (1960) and Dayman (1961). Hyatt (1965) also concluded that measurements of maximum expiratory flow near the mid-vital capacity were most useful in distinguishing subjects with early evidence of obstructive lung disease. Franklin and Lowell (1961a) observed that $MMEF_{50-75\%}$ distinguished most clearly between normal and emphysematous subjects: significant differences between asymptomatic light and heavy smokers have also been found (Franklin and Lowell (1961b)).

There was no difference in $MMEF_{50-75\%}$ between pneumoconiotic and control miners, although any changes due to pneumoconiosis may have been masked by other factors such as smoking. There was a wide variation in individual values, however, which was shown to be well correlated with total aerosol deposition. If measurements of flow at low lung volumes do reflect small airways resistance, this correlation would conform with the known behaviour of airborne particles of about 1μ diameter. Such particles have a high probability of penetration of the upper respiratory tract to the lower airways and pulmonary airspaces. Any obstruction causing generalised small airway narrowing would be likely to result in increased removal of inhaled particles by inertial forces.

The reduction in $FEV_1\%$ and the increase in RV% in subjects with increased deposition strongly suggests that airways obstruction is the primary determinant of the abnormal pattern of aerosol deposition. There was no significant correlation between transfer factor and deposition. It would appear therefore from lung function measurements alone that deposition is increased in subjects with evidence of chronic non-specific lung disease of the obstructive type. This may be caused by exposure either to airborne coal-dust, or to some other occupational airborne hazard, cigarette smoke or air pollution.

(ii) The effects of smoking

In this study $MMEF_{50-75\%}$, which reflects the degree of obstruction or narrowing of the smaller airways, was measured for each subject and it can be seen (Table 11) that smokers had on average an $MMEF_{50-75\%}$ which was 43% lower than the non-smokers. That this is not a short term effect can be observed from the fact that ex-smokers of 1 - 10 years duration had an $MMEF_{50-75\%}$, which was 44% below that of the non-smoking group. Other tests of lung function such as FEV_1, RV% and T_L showed smaller but similar trends. Aerosol deposition was shown to be higher in the smoking group (Table 11), mainly due to their impaired lung function.

In a study of smoking habits at three Scottish collieries, Ashford et al (1968) found that FEV_1 was reduced in smokers in all age groups, although the magnitude of the reduction, about 6% for men aged between 50 and 65 years old, was considerably less than that found in non-mining groups. This could partially be explained by the fact that underground coalworkers could not smoke during their working hours. A similar difference can be found for the groups in this study, 6.7% reduction for smokers aged between 48 and 64 years.

There were considerable differences in the distribution of shape factors between the smoking and non-smoking subjects. Of the 8 non-smokers, six had convex curves and two had concave types. On the other hand only nine (22%) smokers had a convex curve, while 10 (24%) had the concave type and 22 (54%) had the intermediate type of curve. Therefore the majority of smokers showed some kind of abnormality in the shape of their expired aerosol concentration curve, in contrast to the non-smoking group. Ex-smokers were intermediate in this respect with three subjects with convex curves, three with the intermediate type and one with the concave type. As can be seen from Table 11, average deposition for the non-smokers was 18.5% ($\pm$ 4.1%SD) and 21.6% ($\pm$ 3.3%SD) for the smokers, a difference which is just significant ($P < 0.05$)

Although this difference may not be very large, it becomes more significant when taken in relation to the site of aerosol deposition as reflected in the shape of the expired aerosol concentration curve. For a given total deposition value the presence of an abnormal distribution curve probably indicates increased mixing of tidal air and lung air during breathing. This might be associated with a relatively greater deposition of particles within the alveolar spaces. Therefore the smoking habits of an individual miner merit further consideration in relation to the causation of simple pneumoconiosis.

(iii) The presence of respiratory symptoms

The presence of respiratory symptoms, essential to the definition of chronic bronchitis was analysed for this population of coalworkers, in order that a possible relationship with aerosol deposition could be established. Each subject answered a standard questionnaire and from their responses it was possible to state the presence or absence of any of the following six respiratory symptoms.

1. Persistent cough in the morning or during the day for most days for at least 3 months of the year.
2. The production of phlegm in the morning or during the day for most days for at least 3 months of the year.
3. Presence of dyspnoea when walking on level ground (equivalent to grade 3 on the recommended scale of Fletcher et al (1959)).
4. The occurrence of wheezing or whistling in the chest, other than during a cold.
5. Production or aggravation of symptoms by the weather.
6. Presence of a chest illness within the last 3 years which has kept subject off work for more than a week.

It was hoped that the association of the number of symptoms with aerosol deposition could be assessed since they have been shown to be related to lung function, notably FEV_1, $MMEF_{25-75\%}$, VC and RV/TLC % (Hyatt et al 1965). Because of insufficient numbers, it was not possible to establish any clear connection between aerosol deposition or lung function in subjects grouped according to number of symptoms. However, classifying the subjects into 4 groups: (a) with no symptoms; (b) 1 - 2 symptoms; (c) 3 - 4 symptoms and (d) 5 - 6 symptoms, did show a tendency for lung function to deteriorate as the number of symptoms increased (Table 10).

Although $MMEF_{50-75\%}$ and RV/TLC% both showed small consistent deterioration with increasing number of symptoms, aerosol deposition showed no such change. The shape of the expired aerosol concentration curve also showed almost no relationship to the number of symptoms (Table 10).

It is evident that the factors causing mixing of aerosol within the respiratory tract are complex and bear no simple relationship to the presence of respiratory symptoms or to the more simple tests of lung function.

ıg page 38

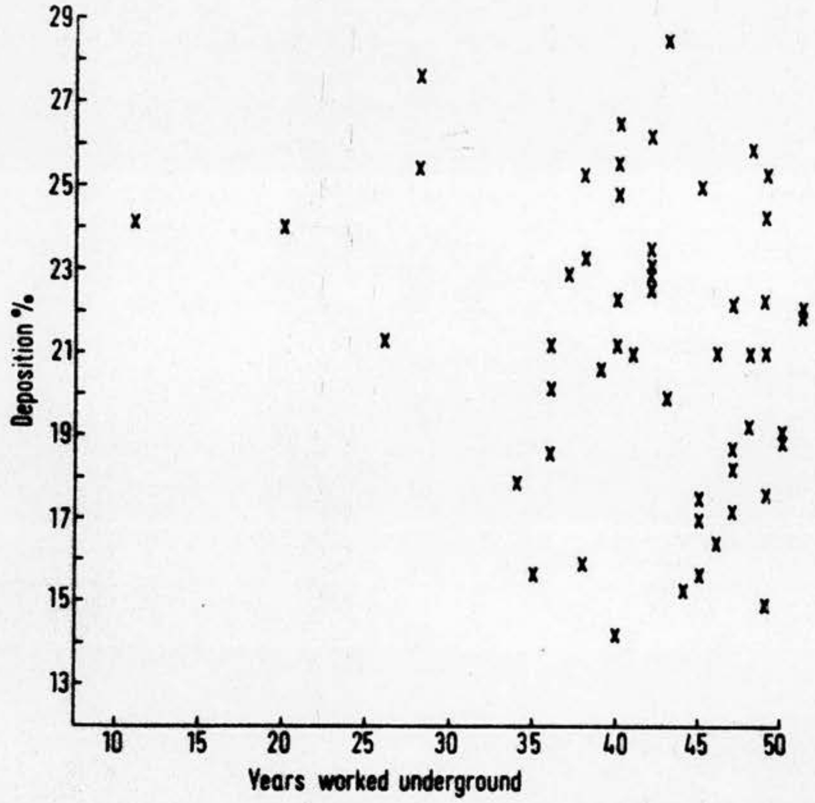

Fig. 26 Effect of years worked underground on total deposition

(iv) Age and years worked underground

It has been well established that the prevalence of pneumoconiosis increases with age and with the number of years spent underground (Fletcher 1955, McCallum et al 1955, McCallum & Newell 1958). It has also been shown (Leatheart 1959, Hyatt et al 1964) that long periods spent underground alter various characteristics of the lung, irrespective of the category of pneumoconiosis. Leathart (1959) showed that lung elastance was increased in a group of elderly faceworkers and that the non-elastic work of breathing, probably caused by bronchial obstruction during expiration, was also frequently increased. Hyatt et all (1964) claimed that pulmonary function, particularly FEV_1 and $MMEF_{25-75\%}$, was impaired following one to ten years underground but was not significantly altered in the course of additional years. The prevalence of respiratory symptoms and bronchitis was lower in those who had worked less than 10 years underground. In a selected group of older men they found that there was functional impairment in those who had worked underground for 10-30 years compared with those who had worked underground for less than 10 years. There was apparently no further deterioration in men who worked underground for more than 30 years.

Most of the subjects in this study had worked underground for between 30 and 50 years and only six had worked less than 30 years underground. The average age was 58.5 years with a range of 48 - 64 years. As a result, any effects on the behaviour of inhaled particles due to age or to length of time spent underground were probably obscured by the narrow range of ages and years of employment.

The effect of the number of years worked underground on total deposition is demonstrated in Fig. 26. It can be seen that there is a very wide spread of deposition values in relation to the relatively narrow range of years spent underground. The average deposition for the five subjects, who worked for less than 30 years underground (three are now surface workers) was 24.5% (range 21.3 - 27.6%), for 15 subjects with between 30 and 40 years underground it was 21.0% and for 32 subjects with more than 40 years underground it was 20.8%.

There was no evident relationship between total deposition and years of underground work when the latter was in the range of 30 - 50 years. There were too few subjects with less than 30 years underground experience to draw any conclusions.

6.5 The significance of the deposition measurements in the pathogenesis of lung disease in coalworkers.

The deposition of aerosol particles in the lungs of coalworkers and its correlation with other factors has been presented in section 6.4: its significance and relationship to other studies can now be discussed.

The most significant finding of this study was that total deposition in this group of coalworkers was not related to the X-ray status of the individual and therefore was not an aetiological factor in simple pneumoconiosis. However, total deposition, which exhibited wide individual variation, was related to airway obstruction. This obstruction was dominated by smoking, and other factors appeared to have little additional effect on airway obstruction, which was shown to be predominantly in the small airways.

Other workers had observed, however, that ventilatory capacity and the mechanical behaviour of the lungs of coalworkers is often more abnormal in miners without pneumoconiosis than in miners with categories 1 and 2 (Carpenter et al 1956; Leathart 1959). These changes are not clearly understood but are believed to be related to long years of work underground and to the fact that emphysema is common in elderly faceworkers.

The work of Heppleston (1947 and 1953) demonstrated that the principal lesion in coalworkers simple pneumoconiosis was focal emphysema of the respiratory bronchioles, whose internal diameter may be increased by a factor of four and which are surrounded by an accumulation of coal dust. This increase in volume may be sufficient to compress the alveolar sacs. In physiological terms it is equivalent to a small increase in dead space.

Gilson and Hugh-Jones (1955) in an extensive study of lung function in Welsh coalminers concluded that a decrease in ventilatory capacity and increased ventilatory requirement during exercise were often present in simple pneumoconiosis. This is consistent with the findings in the present study, since the FEV_1, in the miners with pneumoconiosis was only 83% of predicted normal. However, the FEV_1 in the control group was also slightly below the predicted normal value (Table 3).

A recent major epidemiological survey (Rogan et al - to be published) has now shown that ventilatory capacity is directly related to previous exposure rather than to X-ray status of the individual. The findings of this thesis extend these observations to include measurements of aerosol deposition. It is evident that the presence of simple pneumoconiosis is not in itself, associated with any significant changes in total deposition. Environmental exposure to excessive dust may, however, result in small airways disease as well as in pneumoconiosis and the latter is likely indirectly to be associated with abnormal particle behaviour in the lung.

Until recently little work had been reported on the effect of pathological conditions of the lung on aerosol deposition, although the majority of the more important lung diseases is caused directly or indirectly by inhaled particles.

Palmes et al (1971) have recently reported on the behaviour of half micron diameter particles during breathholding in the lungs of selected patients with emphysema. They have shown that the persistence time of airborne particles in the lungs may be considerably prolonged compared with normal subjects. However, emphysema is always associated with airway obstruction owing to destruction of airway supporting tissue. Therefore increased obstruction is likely to give rise to increased deposition, although the presence of the emphysematous spaces themselves will cause deposition to be decreased. Palmes et al attempted to overcome this problem by studying one group of patients in whom bronchitis predominated and in whom emphysema was variable, and a second group who were primarily emphysematous. They were unable to detect much qualitative or quantitative difference between these two groups.

However, emphysema varies in its location and extent in the respiratory zone of the lung, so that its strategic position may affect the accessibility of aerosol particles to the emphysematous spaces. Thus distal emphysematous spaces may be inaccessible to aerosols, which mainly trace the bulk flow of inspired gases. In the case of focal emphysema in miners the dilated respiratory bronchioles are accessible to an inspired stable aerosol by convective means owing to their more proximal position in the respiratory tract. Dilatation of this region might be expected to increase the percentage of aerosol remaining suspended during the course of a breath. However, it has been observed that the persistence of 0.5μ diameter particles during a breath is generally not very sensitive to changes in lung volume and thus to alveolar and bronchiolar dimensions (Palmes et al 1971).

On the other hand narrowing of the bronchi and bronchioles by excessive secretion of mucus in chronic bronchitis would tend to increase the probability of inertial deposition of particles in these obstructed airways. The present study has demonstrated that subjects with abnormally reduced $MMEF_{50-75\%}$, a measurement which reflects the patency of the smaller airways, have increased deposition of aerosol during steady state breathing.

It has also been demonstrated recently (Lippmann and Albert (1971)) that for aerosols with aerodynamic diameters greater than 2µ deposition in the entire tracheo-bronchial tree is primarily due to impaction, although sedimentation causes significant deposition for particles of the order of 2µ and smaller. They also showed that the current smoking history and existence of lung disease affected regional deposition. The total tracheo-bronchial deposition of particles 1 - 5µ diameter in bronchitics was increased to such an extent that no overlap existed in the range of values for this group when compared with non-smoking healthy controls. Most of this increase was in airways beyond the trachea. This trend was repeated for current cigarette smokers compared with non-smokers, although there was some overlap of data owing to wide variability. The dominant feature was shown to be abnormally high tracheal and/or tracheo-bronchial deposition. Similar results for 2µ particles have been reported by Lourenço (1970).

From these results it is clear that as airways obstruction increases more proximal deposition of larger particles ($>1\mu$) will occur as a result of inertial impaction and less will penetrate to the alveoli. The presence of airways obstruction will also give rise to more mixing of inhaled air with lung air. This would affect the smaller particles, which are uninfluenced by impaction, and more of these would penetrate to the alveolar regions, where accumulation and tissue damage could consequently occur.

It has been suggested (Muir 1970) that the considerable reduction in the amount of aerosol recovered in the exhaled tidal air of bronchitics and asthmatics after a single breath of aerosol could be caused by increased turbulence in the airways or by some form of sequential ventilation. Both increase the apparent amount of mechanical mixing of tidal air with lung air. Normally only 15 - 20% of the tidal air is mixed by this means

(Altshuler et al (1959); Muir (1967)). Unequal ventilation to different regions of the lung may occur causing exchange of particles via collateral channels (e.g. interalveolar pores of Kohn) into otherwise inaccessible regions. In this case some of the inspired aerosol would be irrecoverable - even following a maximum exhalation.

It has been demonstrated that, although the flow pattern in the upper respiratory tract is not laminar (West and Hugh-Jones, 1959; Dekker, 1961 and Jaeger and Matthys 1970), airflow in the more distal bronchial tree is laminar even under conditions of deep, rapid ventilation. However, any obstruction in this region, e.g. mucus plugging, might upset this laminar flow pattern and the resultant mixing could transfer aerosol particles from the axial to the peripheral zone of the airway, thus increasing the chances of eddy deposition and deposition by sedimentation. Taplin et al (quoted by Thomson and Short (1969) and Pircher et al (1965), using a heterogenous aerosol found that aerosol penetration was more restricted than ventilation in chronic bronchitis and asthma and that some was deposited at the site of obstruction giving rise to less penetration and deposition beyond.

The measurements of aerosol deposition presented in this thesis have been concerned only with total deposition within the respiratory system: regional deposition beyond the terminal bronchioles, for example, cannot be directly inferred from the results. However, the curve relating aerosol concentration to expired volume may provide a method of making a qualitative assessment of regional deposition within the lungs. It has already been noted that obstruction in the larger airways of bronchitics and asthmatics gives rise to a proximal shift in the deposition of inhaled particles (Lippmann et al 1971). The results from this study confirm that an abnormal pattern of deposition occurs in subjects with airway obstruction, characterised by the concave shape of the expired aerosol concentration curve in such subjects.

Previous workers (Wilson and La Mer, 1948; Brown et al, 1950 and Altshuler et al 1957) have produced only indirect evidence of regional deposition in human lungs, although variations in upper respiratory tract deposition have been measured (Lippmann et al 1971). Using current techniques it is not possible to assess aerosol deposition quantitatively in each pulmonary region. Therefore much theoretical and experimental work remains to be done in this field before regional deposition measurements in diseased lungs can be attempted.

From the evidence presented in this thesis it would appear that simple pneumoconiosis of coalworkers does not affect the range of deposition of 1μ diameter particles in the lungs of elderly miners, although it may influence the site of deposition depending on the degree of associated bronchitis and emphysema, both of which are found more frequently in pneumoconiotics. This finding may or may not be applicable to particles of different diameter although this awaits further research. It is unlikely that results significantly different to those reported here will be found since Altshuler et al (1957) in a study of normal subjects, found little difference in the relative magnitudes of deposition between individuals for several particle sizes between 0.14μ and 3.2μ diameter.

This study has shown that no relationship exists between simple pneumoconiosis and total deposition of inhaled particles 1μ in diameter. It has also been shown that as the shape of the expired aerosol concentration curve changes from the convex to the concave type total aerosol deposition increases on average and lung function deteriorates. This is probably related to the smoking history of the subject since, although no attempt has been made to correlate degree of deposition with number of cigarettes smoked, it can be seen that smokers on average have a higher total deposition than non-smokers and ex-smokers (Table 11). $MMEF_{50-75\%}$ is also considerably lower for smokers than non-smokers and only 22% of smokers compared with 75% of non-smokers had a convex shape factor. It would therefore appear that little additional information is likely to be obtained about the basic deposition mechanisms in coal-workers by studying the deposition of a range of particle sizes.

The techniques employed in the present study did not allow measurement to be made of clearance of deposited material from the lungs. Since abnormalities of the clearance mechanisms may play an important role in the pathogenesis of the disease, it is clear that studies of particle clearance are required in subjects with dust diseases such as coalworkers' pneumoconiosis. It is apparent that there is a complex interplay of factors involved in the causation of pneumoconiosis in the individual miner. For example, it has even been suggested (Gough 1959) that the presence of bronchitis may protect the lung from pneumoconiosis, since dust free areas have been found in association with bronchitic airways.

It is therefore suggested that total deposition in these experiments is closely related to the function of the small airways and is greater in subjects with airway obstruction. As a result of the findings presented in this thesis it is also suggested that coalworkers' simple pneumoconiosis is unrelated to the breath by breath deposition rate of inspired particles. Jacobsen et al (1971) have found that the progression of pneumoconiosis depends upon the mass concentration of inhaled dust and to the duration of exposure. It is also related to the X-ray category of pneumoconiosis, such that those men who have already developed X-ray changes are more likely to progress to a higher category than those whose X-rays are normal. The present study suggests that the development of pneumoconiosis is unlikely to be related to an initially high rate of dust deposition per se and that the presence of dust in the lungs does not further increase the deposition rate.

CHAPTER 7

SUMMARY AND CONCLUSIONS

It is concluded from the data presented in this thesis that the presence of coalworkers' simple pneumoconiosis is not associated with any change in the total deposition of 1µ diameter particles in the lungs of miners. It was found that deposition was considerably increased in those subjects who had evidence of airways obstruction. The closest correlation was found with those tests of lung function which are thought to indicate disease of the small airways.

Subjects who had high deposition values were easily recognisable due to the abnormal distribution of aerosol in their exhaled air. These subjects had a characteristically concave expired aerosol concentration curve (shape factor), which could be readily distinguished from the normal convex curve. It was possible to categorise each subject by a visual grading of this curve, whose shape was found to be significantly correlated with $MMEF_{50-75\%}$.

Cigarette smoking was shown to be associated with an increased total deposition of aerosol and there was a greater proportion of smokers with abnormal expired concentration curves compared with non-smokers.

These results suggest that the development of pneumoconiosis is unlikely to be related to an initially high rate of dust deposition per se and that the presence of dust in the lungs does not further increase the deposition rate.

ACKNOWLEDGEMENTS

The author wishes to express his thanks to Professor K.W. Donald and to Dr. D.C.F. Muir, under whose supervision this thesis was prepared, and especially to the latter for many invaluable discussions; to Mr. K.F. Sweetland for technical assistance and Miss J.L.L. Baird for typing the manuscript.

My thanks are also due to Mr. R.G. Steele for his assistance in preparing the computer programme, Miss A. Skrimshire and Mr. M.D. Attfield for statistical advice; Mr. G. Murray for designing the electronics necessary for data recording.

Finally I would like to acknowledge both the willingness and patient co-operation of all the coalworkers who took part in this study and also the assistance of the colliery managers and officials of the following collieries in Scotland:- Bilston Glen, Easton, Lady Victoria, Monktonhall and Polkemmet.

R E F E R E N C E S

Albert, R.E., Lippmann, M and Briscoe, W. (1969). Arch. Environ. Health. 18, 738-755

Altshuler, B., Yarmus, L., Palmes, E.D. and Nelson, N. (1957). A.M.A. Arch.Indust.Hyg. 15, 293-303

Altshuler, B., Yarmus, L., Palmes, E.D. and Nelson, N. (1959). J.Appl. Physiol. 14, 321-327

Ashford, J.R., Brown, S., Morgan, D.C. and Rae, S. (1968). Am.Rev. Resp.Dis. 97, 810-826

Beeckmans, J.M. (1965) Canad.J.Physiol.Pharm. 43, 157-172

Brown, C.E. (1931) J.Ind.Hyg.Toxicol. 13,285-291

Brown, C.E. (1931) J.Ind.Hyg.Toxicol. 13, 293-313

Brown, J.H., Cook, K.M., Ney, F.G. and Hatch, T. (1950). Am.J. Public Health 40, 450-458

Camner, P. and Philipson, K. (1971) Symposium on Inhaled Particles (ed. Walton, W.H.) Old Woking, Surrey : Unwin Bros. p.157-163

Carpenter, R.G., Cochrane, A.L., Gilson, J.C. and Higgins, I.T.T. (1956) Brit.J.Ind.Med. 13, 166-176

Collis, E.L. and Gilchrist, J.C. (1928) J. Indust.Hyg. 10, 101.

Cotes, J.E. (1968). Lung Function 2nd edition, Oxford, Blackwell

Cotes, J.E., Houston, K. and Saunders, M.J. (1971). J.Physiol. 22-23P

Crooke-Morgan, D., Pasqual, R.S.H. and Ashford, J.R. (1964). Br.J.prev. Soc.Med. 18, 88.

Cummins, S.L. and Sladden, A.F. (1930). J.Path. and Bact. 33, 1095-1132

Dautrebande, L., Beeckmans, H. and Walkenhorst, W. (1957). A.M.A. Arch.Indust.Health. 16, 179-187

Dautrebande, L., and Walkenhorst, W. (1961). Symposium on Inhaled Particles and Vapours I (ed. C.N. Davies). Oxford, Pergamon p.110-120

Davies, C.N. (1952). Brit.J.Ind.Med. 9, 120.

Davies, C.N. (1964). Ann. Occup.Hyg. 7, 169-183

Dayman, H. (1961). Am.Rev.Resp.Dis. 83, 842-855

Dekker, E. (1961) J.Appl.Physiol. 16, 1060-1064

Dennis, W.L. (1961). Symposium on Inhaled Particles and Vapours I (ed. C.N. Davies) Oxford, Pergamon. p.88

Drinker, P., Thomson, R.M. and Finn, J.L. (1928). J.Ind.Hyg.Toxicol. 10, 13-25

Findeisen, W. (1935). Pflüger's Arch.ges.Physiol. 236, 367-379

Fleisch, A (1925). Pflüger's Arch.ges.Physiol. 209, 713-722

Fletcher, C.M. (1955). A.M.A.Arch.Indust.Health. 11,29-41

Fletcher, C.M., Elmes, P.C., Fairbairn, A.S. and Wood, C.H. (1959) Brit.Med.J. 2, 257

Franklin, W. and Lowell, F.C. (1961a). J.Allergy. 32, 162-168

Franklin, W. and Lowell, F.C. (1961b). Ann.Int.Med. 54, 379-386

Fry, D.L. (1958). Phys.Med.Biol. 3, 174-194

Fry, D.L. and Hyatt, R.E. (1960). Am. J.Med. 29, 672-689

Gilson, J.C. and Hugh-Jones, P. (1955). Med.Res.Counc., Spec.Rep. Ser. 290.

Gough. J. (1940). J.Path.Bact. 51, 277-285

Gough, J. (1959). In :'Modern Trends in Pathology': (ed. D.H. Collins) London, Butterworth

Hadden, G.G., Jones, C.O. and Morgan, D.C. (1967). Inhaled Particles and Vapours II (ed. C.N. Davies). Pergamon, Oxford. p.37-48

Hart, P. d'A. and Aslett, E.A. (1942). Med.Res.Coun.Spec.Rep. Ser.243 H.M.S.O.

Heppleston, A.G. (1947). J.Path.Bact. 59, 453-460

Heppleston, A.G. (1953). J.Path.Bact. 64, 235-246

Hicks, D., Fay, J.W.J., Ashford, J.R. and Rae, S. (1961). National Coal Board, London

Hyatt, R.E. (1961). Am.Rev.Resp.Dis. 83, 676-683

Hyatt, R.E. (1965). Handbook of Physiology : Respiration Vol.II American Physiological Society. Washington. p.1381-1397

Hyatt, R.E., Kistin, A.D. and Mahan, T.K. (1964). Am.Rev.Resp.Dis. 89, 381-401

Hyatt, R.E. Schilder, D.P. and Fry, D.L. (1958). J.Appl.Physiol. 13, 331-336

International Labour Organisation (1958). Occup.Saf.Hlth., 9, 63

International Labour Organisation (1970). International classifaction of radiographs of pneumoconioses (revised (1968) (Occupational Safety and Health Series No. 22). International Labour Office, Geneva

Jacobsen, M., Rae, S., Walton, W.H. and Rogan, J.M. (1971). In Symposium on Inhaled Particles, London (ed. W.H. Walton) Old Woking, Surrey, Unwin Bros. p.903-919

Jaeger, M.J. and Matthys, H. (1970). In Airway Dynamics (ed. A. Bouhuys) Charles C. Thomas, Springfield, Illinois. p.21-32

La Mer, V.K. and Sinclair D. (1943). O.S.R.D. 1668. Div.10-501, 11-M6

Landahl, H.D. (1950). Bull.Math.Biophys. 12, 43-56

Landahl, H.D. (1963). Bull.Math.Biophys. 25, 29-30

Landahl, H.D. and Hermann, R.C. (1948). J.Ind.Hyg.Toxicol. 30, 181-188

Landahl, H.D., Tracewell, T.N. and Lassen, W.H. (1951). A.M.A. Arch. Indust.Hyg. 3, 359-366

Leathart, G.L. (1959). Brit.J.Indust.Med. 16, 153-165

Lehmann, G. (1935). J.Indust.Hyg. 17, 37-40

Liddell, F.D.K. and May, J.D. (1966). Medical Research Memorandum 4 London : National Coal Board

Liddell, F.D.K. and Lindars, D.C. (1969). Brit.J.Indust.Med. 26, 89-100

Lippmann, M.L., Albert, R.E. and Peterson, H.T. (1971). In Symposium on Inhaled Particles, London (ed. W.H. Walton). Old Woking, Surrey, Unwin Bros. p. 105-122

Lourenço, R.V. (1970). Amer.Rev.Resp.Dis. 101, 460-461

McCallum, R.I., Browne, R.C. and Campbell, H (1955). Brit. J.Indust.Med. 12, 279-289

McCallum, R.I. and Newell, D.J. (1958). Brit.J.Indust.Med. 15, 178-187

Medical Research Council (1943). Spec.Rep.Ser. 144. H.M.S.O. London

Medical Research Council (1961). "Instructions for the use of the Short Questionnaire on Respiratory Symptoms, 1960".

Morrow, P.E. (1967). Physiology in the Space Environment. Vol.II. Respiration. National Academy of Sciences, National Research Council, Washington, D.C. p.127

Muir, D.C.F. (1965). Ann.Occup.Hyg. 8, 233-238

Muir, D.C.F. (1966). Ph.D. Thesis. University of London

Muir, D.C.F. (1967). J.Appl.Physiol. 23, 210-214

Muir, D.C.F. (1970). In 'Airway Dynamics' (ed. A. Bouhuys). Charles C. Thomas. Springfield, Illinois. P.319-325

Muir, D.C.F. and Davies, C.N. (1967). Ann.Occup.Hyg. 10, 161-174

Palmes, E.D. Goldring, R.M., Wang, C.S. and Altshuler, B. (1971). In Symposium on Inhaled Particles (ed. W.H. Walton). Old Woking, Surrey. p.123-130

Pircher, F.J., Temple, I.R., Kirsch, W.J. and Reeves, R.J. (1965). Am.J. Roentgenol.Radium Therapy, Nucl.Med. 94, 807-814

Policard, A., quoted by Hatch, T.F. and Gross, P. (1964). In : Pulmonary Deposition and Retention of Inhaled Aerosols. Academic Press. New York. p.119

Rae, S., Walker, D.D. and Attfield, M.D. (1971). In : Symposium on Inhaled Particles (ed. W.H. Walton). Old Woking, Surrey. p.883-896

Rivers, D., Wise, M.E., King, E.J. and Nagelschmidt, G. (1960). Brit.J. Ind.Med. 17, 87-108

Rogan, J.M., Ashford, J.R., Chapman, P.J., Duffield, D.P., Fay, J.W.J. and Rae, S. (1961). Brit.Med.J. 1, 1337-1342

Rogan, J.M., Attfield, M.D., Jacobsen, M., Rae, S., Walker, D.D. and Walton W.H. (1973). Brit.J.Ind.Med. In press

Rossiter, C.E., Rivers, D., Bergmann, I., Casswell, C. and Nagelschmidt, G. (1967). Inhaled Particles and Vapours II (ed. C.N. Davies). Oxford, Pergamon. p.419-437

Sinclair, V.K. (1950). 'Handbook on Aerosols'. Atomic Energy Commission, Washington, p.84

Swift, D.L. (1967). Ann.Occup.Hyg. 10, 337-348

Thomson, M.L. and Short, M.D. (1969). J.Appl.Physiol. 26, 535-539

Van Wijk, A.M. and Patterson, H.S. (1940). J.Ind.Hyg.Toxicol. 22, 31-35

Watson, H.H. (1936). Trans.Inst.Min. Mett. 46, 176-187

Weibel, E.R. (1963). Morphometry of the Human Lung. Berlin, Springer.

West, J.B. and Hugh-Jones, P. (1959). J.Appl.Physiol. 14, 753-759

Wilson, I.B. and La Mer, V.K. (1948). J.Ind.Hyg.Toxicol. 30, 265-280

Wooding, E.R., quoted by Muir, D.C.F., Ann.Occup.Hyg. (1965), 8, 233-238